09/ 964,161

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PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS	4	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS	5	FEB 05	German (DE) application and patent publication number format changes
NEWS	6	MAR 03	MEDLINE and LMEDLINE reloaded
NEWS	7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS	8	MAR 03	FRANCEPAT now available on STN
NEWS	9	MAR 29	Pharmaceutical Substances (PS) now available on STN
NEWS	10	MAR 29	WPIFV now available on STN
NEWS	11	MAR 29	No connect hour charges in WPIFV until May 1, 2004
NEWS	12	MAR 29	New monthly current-awareness alert (SDI) frequency in RAPRA

NEWS EXPRESS	MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 13 APRIL 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:43:56 ON 20 APR 2004

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 13:44:06 ON 20 APR 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

09/ 964,161

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 19 APR 2004 HIGHEST RN 676225-08-4
DICTIONARY FILE UPDATES: 19 APR 2004 HIGHEST RN 676225-08-4

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\STNEXP4\QUERIES\09964161.str

chain nodes :
7 8 9 10 11 12 15 16 17
ring nodes :
1 2 3 4 5 6
chain bonds :
4-7 7-8 8-9 8-15 9-10 10-11 10-12 15-16 15-17
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
8-9 9-10 10-11 10-12 15-16 15-17
exact bonds :
4-7 7-8 8-15
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 :

G1:O,N

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:Atom 12:CLASS 15:CLASS 16:CLASS 17:CLASS
Generic attributes :
11:
Number of Carbon Atoms : 7 or more
Type of Ring System : Polycyclic

Element Count :
Node 11: Limited
C,C9-13
O,O0-3
S,S0-3
N,N0-5

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L1      STRUCTURE UPLOADED

=> s l1 ful
FULL SEARCH INITIATED 13:44:24 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 643968 TO ITERATE

 47.2% PROCESSED  304013 ITERATIONS                                943 ANSWERS

 62.1% PROCESSED  400000 ITERATIONS                               1110 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.33

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **INCOMPLETE**
PROJECTED ITERATIONS:       643968 TO   643968
PROJECTED ANSWERS:            1661 TO     1913

L2         1110 SEA SSS FUL L1

=> d l1
L1 HAS NO ANSWERS
L1              STR
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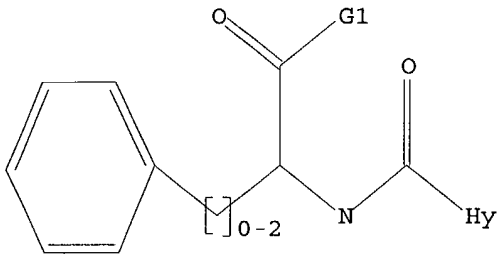


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G1 O,N


Structure attributes must be viewed using STN Express query preparation.


=> s l2
SAMPLE SEARCH INITIATED 13:46:09 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -  32383 TO ITERATE

  3.1% PROCESSED    1000 ITERATIONS                                  3 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **INCOMPLETE**
                        BATCH   **INCOMPLETE**
PROJECTED ITERATIONS:       636917 TO   658403
PROJECTED ANSWERS:            1351 TO     2533

L3            3 SEA SSS SAM L1

=> file caplus
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                   ENTRY    SESSION
```

09/ 964,161

FULL ESTIMATED COST 156.68 156.89

FILE 'CAPLUS' ENTERED AT 13:46:39 ON 20 APR 2004
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 20 Apr 2004 VOL 140 ISS 17
FILE LAST UPDATED: 19 Apr 2004 (20040419/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l2
L4 261 L2

=> d l4 1- ibib abs fhitstr
YOU HAVE REQUESTED DATA FROM 261 ANSWERS - CONTINUE? Y/(N):y

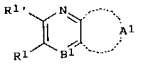
L4 ANSWER 1 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:252486 CAPLUS
TITLE: Preparation of quinoline and naphthyridine derivatives as HIV integrase inhibitors
INVENTOR(S): Murai, Hitoshi; Endo, Takeshi; Kurose, Noriyuki; Taishi, Teruhiko; Yoshida, Hiroshi
PATENT ASSIGNEE(S): Shionogi & Co., Ltd., Japan
SOURCE: PCT Int. Appl., 396 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

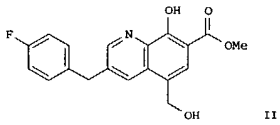
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004024693	A1	20040325	WO 2003-JP10212	20030811

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2002-235582 A 20020813
JP 2002-245772 A 20020826
JP 2003-121726 A 20030425
JP 2003-270863 A 20030704

GI


I

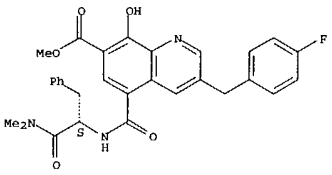

II

AB The title compds. I [wherein B1 = N or (un)substituted CH; R1 = H, (un)substituted alkyl, alkenyl, etc.; R1' = H, halo, NO2, OH, CO2H, (un)substituted alkoxycarbonyl, alkyl, alkoxy, etc.; A1 = (un)substituted -CH=CH-CH=CH-, -CH=CH-CH=N-, -CH=CH-N=CH-, -CH=CH-O-CH2-, -CH=CH-CH2-O-, or -CH=CH-O-] or prodrugs, solvates, or pharmaceutically acceptable salts thereof are prepared as HIV integrase inhibitors. For example, the compound II was prepared in a multi-step synthesis. II showed inhibitory activity with IC50 of 0.071 μg/mL against integrase. Formulations containing I as an active ingredient were also described.

IT **675611-88-8P**

L4 ANSWER 1 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of quinoline and naphthyridine derivs. as HIV integrase inhibitors)
RN 675611-88-8 CAPLUS
CN INDEX NAME NOT YET ASSIGNED

Absolute stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:203814 CAPLUS
DOCUMENT NUMBER: 140:253449
TITLE: Preparation of heterocyclylcarboxamides as oxytocin inhibitors
INVENTOR(S): Armour, Duncan Robert; Bell, Andrew Simon; Edwards, Paul John; Ellis, David; Hepworth, David; Lewis, Mark Llewellyn; Smith, Christopher Ronald
PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.
SOURCE: PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004020414	A1	20040311	WO 2003-IB3705	20030813

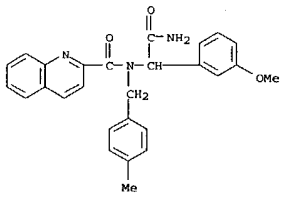
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2002-19961 A 20020828

AB R1CON[(CH2)xR2]C(R4)[(CH2)yR3](CH2)zR5 [R1 = (substituted) Ph, heteroaryl; R2 = (substituted) Ph, OPh, cycloalkyl, heteroaryl, heterocyclyl, etc.; R3 = (substituted) (fused) Ph, heterocyclyl, heteroaryl, R6, etc.; R4 = H, Me; R5 = CONH2, NH2, OH, R6, NHR6, OR6, CONHR6, (substituted) heteroaryl, etc.; R6 = alkyl; x, y, z = 0-2], were prepared Thus, 4-chlorobenzylamine, o-tolualdehyde, 2-aminonicotinic acid, and (4-isocyanocyclohex-3-enyl)benzene (preparation given) were stirred in MeOH/cyclohexane to give a residue which was stirred in aqueous HCl/THF to give 2-amino-N-[2-amino-1-(2-methylphenyl)-2-oxoethyl]-N-(4-chlorobenzyl)nicotinamide. Title compds. at 10 μM gave >70% inhibition of oxytocin.

IT **669087-02-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclylcarboxamides as oxytocin inhibitors)
RN 669087-02-9 CAPLUS
CN 2-Quinolinecarboxamide, N-[2-amino-1-(3-methoxyphenyl)-2-oxoethyl]-N-[(4-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:143094 CAPLUS
DOCUMENT NUMBER: 140:199743
TITLE: Preparation of substituted (2S)-(arylamino)-3-(biphenyl-4-yl)propionic acids as antagonists of factor IX for inhibiting the intrinsic pathway of blood coagulation
INVENTOR(S): Mjalli, Adnan M. M.; Andrews, Robert C.; Guo, Xiao-chuan; Christen, Daniel Peter; Gohimmukkula, Devi Reddy; Huang, Guoxiang; Rothlein, Robert; Tyagi, Sameer; Yaramasu, Tripura; Behme, Christopher
PATENT ASSIGNEE(S): Transtech Pharma, Inc., USA
SOURCE: PCT Int. Appl., 326 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

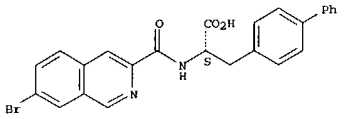
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004014844	A2	20040219	WO 2003-US25045	20030808

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-402272P P 20020809
OTHER SOURCE(S): MARPAT 140:199743
AB The title compds. Ar2XCH(VAr1)(CH2)cG [I; c = 0-2; G = H, CO2R1, CH2OR1, COR1, CR1:NOR2, an acid isostere (wherein R1, R2 = H, alkyl, aryl, etc.); V = (CH2)bO(CH2)a, (CH2)bNR7(CH2)a, (CH2)bO, (CH2)bNR7, (CH2)a, a bond (a = 0-2; b = 1-2; R7 = H, alkyl, aryl, etc.); X = NR8, COR8, NR8CO, etc. (R8 = H, alkyl, aryl, etc.); Ar1 = (un)substituted aryl, heteroaryl, cycloalkylaryl, etc.; Ar2 = (un)substituted aryl or heteroaryl], useful as antagonists, or more preferably, partial antagonists of factor IX and thus, may be used to inhibit the intrinsic pathway of blood coagulation, were prepared Thus, reacting Me 2-L-amino-3-biphenyl-4-yl-propionate with isoquinoline-3-carboxylic acid followed by hydrolysis afforded 81% 3-biphenyl-4-yl-(2S)-[(isoquinoline-3-carbonyl)amino]propionic acid. The compds. I inhibit factor IX with IC50 of less than 30 μM, and are useful in a variety of applications including the management, treatment and/or control of diseases caused in part by the intrinsic clotting pathway utilizing factor IX. Such diseases or disease states include stroke, myocardial infarction, aneurysm surgery, and deep vein thrombosis associated with surgical procedures, long periods of confinement, and acquired or inherited pro-coagulant states. The pharmaceutical composition comprising the compound I is claimed.
IT **660823-98-3P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

L4 ANSWER 3 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of substituted (2S)-(arylamino)-3-(biphenyl-4-yl)propionic acids as antagonists of factor IX for inhibiting the intrinsic pathway of blood coagulation)
RN 660823-98-3 CAPLUS
CN [1,1'-Biphenyl]-4-propanoic acid, α-[[(7-bromo-3-isoquinolinyl)carbonyl]amino]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



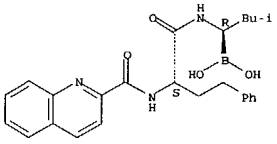
L4 ANSWER 4 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:120719 CAPLUS
DOCUMENT NUMBER: 140:175176
TITLE: Use of a proteasome inhibitor in the treatment of endothelial dysfunction and/or in a low-dose proteasome inhibitor therapy
INVENTOR(S): Stangl, Verena; Stangl, Karl; Lorenz, Mario
PATENT ASSIGNEE(S): Charite-Universitatsmedizin Berlin, Germany
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004012732	A2	20040212	WO 2003-EP8495	20030731

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2002-17234 A 20020731
AB The invention discloses the use of a proteasome inhibitor for the manufacture of a medicament for the prevention, onset therapy, acute therapy, and/or regression of diseases associated with endothelial dysfunction. The invention also discloses the use of a proteasome inhibitor as a low-dose treatment.
IT **179324-59-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(proteasome inhibitor in treatment of endothelial dysfunction and/or in low-dose proteasome inhibitor therapy)
RN 179324-59-5 CAPLUS
CN Boronic acid, [(1R)-3-methyl-1-[[(2S)-1-oxo-4-phenyl-2-[(2-quinolinylcarbonyl)amino]butyl]amino]butyl]- (9CI) (CA INDEX NAME)

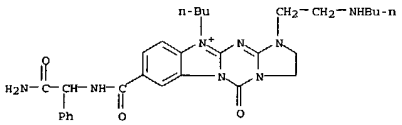
Absolute stereochemistry.



L4 ANSWER 5 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:102765 CAPLUS
DOCUMENT NUMBER: 140:270821
TITLE: Halogenoalkyl Isocyanates as Bifunctional Reagents in an Aza-Wittig/Heterocyclization Reaction on the Solid Phase: Efficient Entry into New Tetracyclic Benzimidazole Systems
AUTHOR(S): Hoesl, Cornelia E.; Nefzi, Adel; Houghten, Richard A.
CORPORATE SOURCE: Torrey Pines Institute for Molecular Studies, San Diego, CA, 92121, USA
SOURCE: Journal of Combinatorial Chemistry (2004), 6(2), 220-223
CODEN: JCCHFF; ISSN: 1520-4766
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An efficient one-pot procedure for the solid-phase synthesis of new tetracyclic 1,3,5-triazino[1,2-a]benzimidazolium derivs. starting from resin-bound benzimidazoles is described. The synthetic strategy involves an unprecedented one-pot aza-Wittig/heterocyclization/substitution reaction sequence using halogenoalkyl isocyanates. The structure of the tetracyclic ring system was determined by two-dimensional NMR expts. and X-ray anal.
IT **673461-98-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid-phase synthesis of 1,3,5-triazino[1,2-a]benzimidazolium derivs. via one-pot aza-Wittig/heterocyclization/substitution reaction sequence using halogenoalkyl isocyanates)
RN 673461-98-8 CAPLUS
CN 1H,5H-Imidazo[2',1':4,5][1,3,5]triazino[1,2-a]benzimidazolium, 8-[[(2-amino-2-oxo-1-phenylethyl)amino]carbonyl]-11-butyl-1-[2-(butylamino)ethyl]-2,3-dihydro-5-oxo-, salt with trifluoroacetic acid (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 673461-97-7
CMF C30 H39 N8 O3



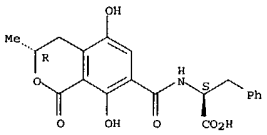
CM 2

CRN 14477-72-6
CMF C2 F3 O2

L4 ANSWER 5 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:56093 CAPLUS
DOCUMENT NUMBER: 140:248526
TITLE: Ochratoxin A: Lack of Formation of Covalent DNA Adducts
AUTHOR(S): Mally, Angela; Zepnik, Herbert; Wanek, Paul; Eder, Erwin; Dingley, Karen; Ihmels, Heiko; Voelkel, Wolfgang; Dekant, Wolfgang
CORPORATE SOURCE: Institut fuer Toxikologie, Universitaet Wuerzburg, Wuerzburg, 97078, Germany
SOURCE: Chemical Research in Toxicology (2004), 17(2), 234-242
CODEN: CRTOEC; ISSN: 0893-228X
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The mycotoxin ochratoxin A (OTA) is a potent nephrotoxin and renal carcinogen in rodents. However, the mechanism of OTA-induced tumor formation is unknown and conflicting results have been obtained regarding the potential of OTA to bind to DNA. OTA is poorly metabolized, and no reactive intermediates capable of interacting with DNA have been detected in vitro or in vivo. Recently, a hydroquinone/quinone redox couple and a carbon-bonded OTA-deoxyguanosine (OTA-dG) adduct formed by electrochem. oxidation and photoreaction of OTA have been reported and suggested to be involved in OTA carcinogenicity. This study was designed to characterize the role of DNA binding and to determine if formation of these derivs. occurs in vivo and in relevant activation systems in vitro using specific and sensitive methods. Horseradish peroxidase activation of OTA and its dechlorinated analog ochratoxin B (OTB) yielded ochratoxin A-hydroquinone (OTHQ), but the postulated OTA-dG adduct was not detectable using LC-MS/MS. In support of this, no OTA-related DNA adducts were observed by 32P-postlabeling. In vivo, only traces of OTHQ were found in the urine of male F344 rats treated with high doses of OTA (2 mg/kg body wt) for 2 wk, suggesting that this metabolite is not formed to a relevant extent. In agreement with the in vitro data, OTA-dG was not detected by LC-MS/MS in liver and kidney DNA extracted from treated animals. In addition, DNA binding of OTA and OTB was assessed in male rats given a single dose of 14C-OTA or 14C-OTB using accelerator mass spectrometry, a highly sensitive method for quantifying extremely low concns. of radiocarbon. The 14C content in liver and kidney DNA from treated animals was not significantly different from controls, indicating that OTA does not form covalent DNA adducts in high yields. In summary, the results presented here demonstrate that DNA binding of OTA is not detectable with sensitive anal. and is unlikely to represent a mechanism for OTA-induced tumor formation.

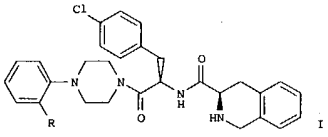
IT **205034-32-8**
RL: FMU (Formation, unclassified); FORM (Formation, nonpreparative)
(DNA binding of ochratoxin A is not detectable with sensitive anal. and is unlikely to represent a mechanism for OTA-induced tumor formation)

RN 205034-32-8 CAPLUS
CN L-Phenylalanine, N-[[(3R)-3,4-dihydro-5,8-dihydroxy-3-methyl-1-oxo-1H-2-benzopyran-7-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 7 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:45782 CAPLUS
DOCUMENT NUMBER: 140:253536
TITLE: Synthesis and Structure-Activity Relationships of Novel Arylpiperazines as Potent and Selective Agonists of the Melanocortin Subtype-4 Receptor
AUTHOR(S): Richardson, Timothy I.; Ornstein, Paul L.; Briner, Karin; Fisher, Matthew J.; Backer, Ryan T.; Biggers, C. Kelly; Clay, Michael P.; Emmerson, Paul J.; Hertel, Larry W.; Hsiung, Hansen M.; Husain, Saba; Kahl, Steven D.; Lee, Jonathan A.; Lindstrom, Terry D.; Martinelli, Michael J.; Mayer, John P.; Mullaney, Jeffery T.; O'Brien, Thomas P.; Pawlak, Joseph M.; Revell, Kevin D.; Shah, Jikesh; Zgombick, John M.; Herr, R. Jason; Melekhov, Alex; Sampson, Peter B.; King, Chi-Hsin R.
CORPORATE SOURCE: Lilly Research Laboratories, A Division of Eli Lilly and Company Lilly Corporate Center, Indianapolis, IN, 46285, USA
SOURCE: Journal of Medicinal Chemistry (2004), 47(3), 744-755
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



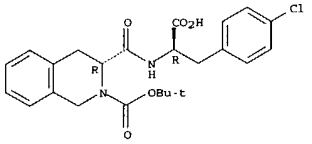
I

AB The melanocortin receptors have been implicated as potential targets for a number of important therapeutic indications, including inflammation, sexual dysfunction, and obesity. (3R)-N-[(1R)-2-[4-[2-(Aminosulfonyl)phenyl]-1-piperazinyl]-1-[(4-chlorophenyl)methyl]-2-oxoethyl]-1,2,3,4-tetrahydro-3-isoquinolinecarboxamide (I; R = H2NSO2) an arylpiperazine attached to dipeptide H-D-Tic-D-p-Cl-Phe-OH, as a novel melanocortin subtype-4 receptor (MC4R) agonist through iterative directed screening of nonpeptidyl G-protein-coupled receptor biased libraries. Structure-activity relationship (SAR) studies demonstrated that substitutions at the ortho position of the aryl ring improved binding and functional potency. For example, the o-isopropyl-substituted compound I (R = isopropyl) (Ki = 720 nM) possessed 9-fold better binding affinity compared to the unsubstituted aryl ring (Ki = 6600 nM). Sulfonamide I (R = MeSO2NH) (II) (Ki = 220 nM) fills this space with a polar substituent, resulting in a further 2-fold improvement in binding affinity. The most potent compds. such as the dimethylamine derivative I (R = Me2NCH2) (Ki = 60 nM) contain a basic group at this position. Basic heterocycles such as the imidazole I [R = (1H-imidazol-1-yl)methyl] (Ki = 110 nM) were similarly effective. Good oral bioavailability for sulfonamide II was also demonstrated.

IT **252008-71-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

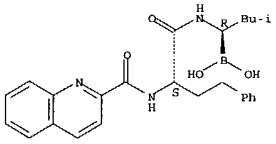
L4 ANSWER 7 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(Reactant or reagent)
(prepn. and structure-activity relationship of {{arylpiperazinyl}[(chlorophenyl)methyl]oxoethyl}tetrahydroisoquinoline carboxamide derivs. as selective melanocortin subtype-4 receptor agonists)
RN 252008-71-2 CAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3-[[[(1R)-1-carboxy-2-(4-chlorophenyl)ethyl]amino]carbonyl]-3,4-dihydro-, 2-(1,1-dimethylethyl) ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:41297 CAPLUS
DOCUMENT NUMBER: 140:105236
TITLE: Proteasome inhibitors for the treatment of herpesviridae-infected individuals
INVENTOR(S): Prosch, Susanne; Volk, Hans Dieter; Kruger, Detlev
PATENT ASSIGNEE(S): Universitatsklinikum Charite der Humboldt-Universitat zu Berlin Technologietrans Ferstelle, Germany
SOURCE: PCT Int. Appl., 47 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004749	A1	20040115	WO 2003-EP7062	20030702

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: EP 2002-14728 A 20020703
AB The invention discloses the use of a substance or composition comprising one or more proteasome inhibitors for the manufacture of a medicament for the treatment of an individual infected with a virus selected from the group comprising varicella zoster virus, human cytomegalovirus, human herpesvirus 6 and 7 and Epstein-Barr virus and Karposi's sarcoma herpesvirus. The invention further discloses methods for treatment of individuals infected with a virus selected from the group comprising varicella zoster virus, human cytomegalovirus, human herpesvirus 6 and 7 and Epstein-Barr virus and Karposi's sarcoma herpesvirus.
IT **179324-59-5**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(proteasome inhibitors for treatment of herpesviridae infection)
RN 179324-59-5 CAPLUS
CN Boronic acid, [(1R)-3-methyl-1-[[(2S)-1-oxo-4-phenyl-2-[(2-quinolinylcarbonyl)amino]butyl]amino]butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

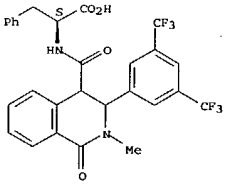
L4 ANSWER 9 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:41276 CAPLUS
DOCUMENT NUMBER: 140:105251
TITLE: 3,4-Dihydroisoquinolin-1-one derivatives as inducers of apoptosis
INVENTOR(S): Gangloff, Anthony R.; Litvak, Joane; Pararajasingham, Keith; Sperandio, David
PATENT ASSIGNEE(S): Axys Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004004727	A1	20040115	WO 2003-US21102	20030703

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-394094P P 20020703
OTHER SOURCE(S): MARPAT 140:105251
AB The invention discloses 3,4-dihydroisoquinolin-1-one derivs. that are activators of caspases and inducers of apoptosis, as well as pharmaceutical compns. comprising these compds., and methods for treating cancer using these compds. Preparation of selected compds. of the invention is included.
IT **646028-31-1**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dihydroisoquinolinone derivs. as inducers of apoptosis, and use for cancer treatment)
RN 646028-31-1 CAPLUS
CN L-Phenylalanine, N-[[3-[3,5-bis(trifluoromethyl)phenyl]-1,2,3,4-tetrahydro-2-methyl-1-oxo-4-isoquinolinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 9 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

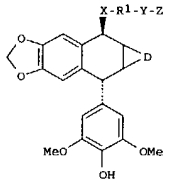
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:2899 CAPLUS
DOCUMENT NUMBER: 140:27711
TITLE: Preparation of etoposide aglycon analogs as antitumor agents and DNA topoisomerase II inhibitors
INVENTOR(S): Lee, Kuo-Hsiung; Xiao, Zhiyan; Bastow, Kenneth F.
PATENT ASSIGNEE(S): University of North Carolina at Chapel Hill, USA
SOURCE: PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000859	A2	20031231	WO 2003-US19629	20030620
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 6566393	B1	20030520	US 2002-177147	20020621
US 2004006126	A1	20040108	US 2003-349351	20030122

PRIORITY APPLN. INFO.: US 2002-177147 A 20020621
US 2003-349351 A 20030122
OTHER SOURCE(S): MARPAT 140:27711
GI



I

AB Etoposide amino acid analogs I (X = O, S, NH, CO, CH:N, CH2NH; R1 = covalent linkage between X and Y, alkyl, alkenyl, (un)substituted Ph; Y = NHCO, CONH; Z = CHR2(CH2)nR3, R2 = CO2H, NH2, ester, etc., R3 = alkyl,

L4 ANSWER 10 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

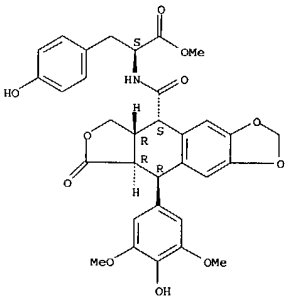
alkenyl, aryl, n= 0-2; D = CH2OC(O), CH2OC(:CH2), CH2CH2C(O), CH2OCH2, CH2OC(S), CH2O(SO2)OCH2, etc.) were prepd. as DNA topoisomerase II inhibitors. Thus, 4'-O-demethyl-4β-[4''-(methyl-L-tyrosine-N-carbonyl)anilino]-4-deoxy-podophyllotoxin (II) and 4'-O-demethyl-4β-[4''-(methyl-L-tryptophan-N-carbonyl)anilino]-4-deoxypodophyllotoxin were prepd. from podophyllotoxin and their pharmaceutical activity evaluated. The antitumor ED50 of II against A 549 human cell line was 2.4 μM. Cancer is selected from the group consisting of skin cancer, lung cancer, Kaposi's sarcoma, testicular cancer, lymphoma, leukemia, esophageal cancer, stomach cancer, colon cancer, breast cancer, endometrial cancer, ovarian cancer, central nervous system cancer, liver cancer and prostate cancer.

IT **527678-17-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of etoposide amino acid analogs as DNA topoisomerase II inhibitors)

RN 527678-17-7 CAPLUS

CN L-Tyrosine, N-[[(5S,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 11 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2004:2730 CAPLUS
DOCUMENT NUMBER: 140:71043
TITLE: Combination treatment for depression and anxiety by NK1 and NK3 antagonists
INVENTOR(S): Sobolov-Jaynes, Susan Beth; Lowe, John Adams, III; McLean, Stafford
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004000355	A1	20031231	WO 2003-IB2516	20030610
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004006135	A1	20040108	US 2003-386582	20030312

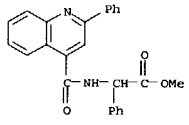
PRIORITY APPLN. INFO.: US 2002-389975P P 20020619
OTHER SOURCE(S): MARPAT 140:71043

AB The invention discloses a method for treating depression or anxiety in a mammal, including a human, by administering to the mammal a CNS-penetrant NK1 receptor antagonist (e. g., a substance P receptor antagonist) in combination with an NK3 antagonist agent. It also relates to pharmaceutical compns. containing a pharmaceutically acceptable carrier, a CNS-penetrant NK1 receptor antagonist and an NK3 antagonist.

IT **174635-51-9**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NK1 and NK3 antagonist combination treatment for depression and anxiety)

RN 174635-51-9 CAPLUS

CN Benzeneacetic acid, α-[[(2-phenyl-4-quinolinyl)carbonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:951028 CAPLUS
DOCUMENT NUMBER: 140:16715
TITLE: Preparation of azepinoindole and pyridoindole derivatives as modulators of farnesoid X and/or orphan nuclear receptors
INVENTOR(S): Martin, Richard; Wang, Tie-Lin; Platt, Brenton Todd; Gu, Xiao-Hui; Griffith, Ronald
PATENT ASSIGNEE(S): X-Ceptor Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 268 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003099821	A1	20031204	WO 2003-US16767	20030527

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004023947	A1	20040205	US 2003-447302	20030527

PRIORITY APPLN. INFO.: US 2002-383574P P 20020524
OTHER SOURCE(S): MARPAT 140:16715
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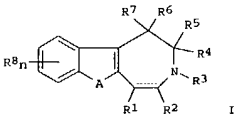

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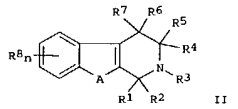


II

L4 ANSWER 12 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

AB The present invention is directed to azepinoindole and pyridoindole derivs. (shown as I and II; variables defined below; e.g. Et 1,2,3,6-tetrahydroazepino[4,5-b]indole-5-carboxylate). These compds. were used in pharmaceutical compns. and methods for modulating the activity of farnesoid X receptor and/or orphan nuclear receptors. A farnesoid X receptor/ECREx7 co-transfection assay and a TR-FRET assay were used to establish the EC50/IC50 values for potency and percent activity or inhibition for efficacy; efficacy defines the activity of a compound relative to a high control (chenodeoxycholic acid, CDCA) or a low control (DMSO/vehicle). Most of the compds. disclosed and tested exhibited activity in at least one of the assays (EC50 or IC50 <10 μM); most showed activity at <1 μM, e.g. Pr 3-(4-fluorobenzoyl)-2-methyl-1,2,3,6-tetrahydroazepino[4,5-b]indole-5-carboxylate exhibited agonist activity <1 μM EC50 and >100 % efficacy and 8-(3-cyclopropyl-1-methylureido)-3-(4-fluorobenzoyl)-1,1-dimethyl-1,2,3,6-tetrahydroazepino[4,5-b]indole-5-carboxylic acid Et ester exhibited antagonist activity with IC50 <100 nM and 100 % inhibition. Although the methods of preparation are not claimed, 74 example prepns. of I and II and characterization data for many more I and II are included. For I and II: n = 0-4; A is -N(R9)-, -O- or -S(O)t- (t = 0-2); R1 and R2 = H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, aralkyl, heteroaralkyl, -OR14, -SR14, -N(R15)R16, -N(R15)S(O)2R43; -N(R17)N(R15)R16, -N(R17)N(R15)S(O)2R43, -C(O)R18, -C(O)OR14, -C(S)OR14, -C(O)SR14, -C(O)N(R15)R16, -C(O)N(R15)S(O)2R43, -C(O)N(R15)N:R16 and -C(O)N(R17)N(R15)R16; or -C(O)N(R17)N(R15)S(O)2R43; or R1 and R2, together with the atom to which they are attached, form a cycloalkyl, heterocyclyl, aryl, or heteroaryl ring. R3 is H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroaralkyl, -C(O)R10, -C(O)OR10, -S(O)2R10, -C(O)N(R11)R12, -C(O)N(R11)S(O)2R43, -C(O)N(R13)N(R11)R12, -C(O)N(R13)N(R11)S(O)2R43, -N(R13)C(O)R10, -N(R13)C(O)N(R11)R12, -N(R13)C(O)N(R11)S(O)2R43, -N(R10)C(O)N(R13)N(R11)R12, -N(R10)C(O)N(R13)N(R11)S(O)2R43, -N(R13)C(O)OR10, -P(O)OR10, or -P(O)(OR19)OR12. R4, R5, R6 and R7 = H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, aralkyl, heteroaralkyl, -OR14, -SR14, -S(O)2R14, -N(R15)R16, -N(R15)S(O)2R43, -C(O)R18, -C(O)OR20, -C(O)N(R21)R22, -C(O)N(R21)S(O)2R43; -C(O)N(R42)N(R21)R22; or -C(O)N(R42)N(R21)S(O)2R43; or R4 and R5, or R4 and R6, or R4 and R7, or R5 and R6, or R5 and R7, or R6 and R7, together with the C atom to which they are attached, form a cycloalkyl, heterocyclyl, or cycloalkenyl ring, or together form a double bond and the others of R4, R5, R6 and R7 are as described above; or R6 and R7 together form an oxo, thioxo, imine, oxime or a hydrazone, or R6 and R7, together with the C atom to which they are attached, form an exocyclic double bond, and R4 and R5 are as described above. R8 = alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, halo, pseudohalo, cyano, nitro, -C(O)OR23, -C(O)N(R24)R25, -C(O)N(R24)S(O)2R43, -C(O)R26, -OR27, -SR27, -C(S)OR23, -C(O)SR23, -N(R28)R29, and -N(R28)S(O)2R43, or two adjacent R8 groups, together with the carbons to which they are attached, form an aryl, cycloalkyl, heterocyclyl or heteroaryl; addnl. details including provisos are given in the claims.

IT **629667-63-6P**

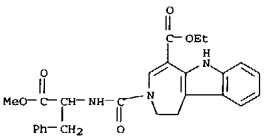
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(drug candidate; preparation of azepinoindole and pyridoindole derivs. as modulators of farnesoid X and/or orphan nuclear receptors)

L4 ANSWER 12 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 629667-63-6 CAPLUS

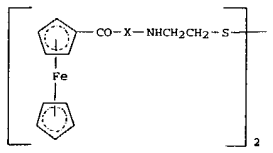
CN Azepino[4,5-b]indole-5-carboxylic acid, 1,2,3,6-tetrahydro-3-[[[2-methoxy-2-oxo-1-(phenylmethyl)ethyl]amino]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:946309 CAPLUS
DOCUMENT NUMBER: 140:128675
TITLE: Electrochemical and Surface Study of Ferrocenoyl Oligopeptides
AUTHOR(S): Bediako-Amoa, Irene; Sutherland, Todd C.; Li, Chen-Zhong; Silerova, Roberta; Kraatz, Heinz-Bernhard
CORPORATE SOURCE: Department of Chemistry, University of Saskatchewan, Saskatoon, SK, S7N 5C9, Can.
SOURCE: Journal of Physical Chemistry B (2004), 108(2), 704-714
CODEN: JPCBFK; ISSN: 1520-6106
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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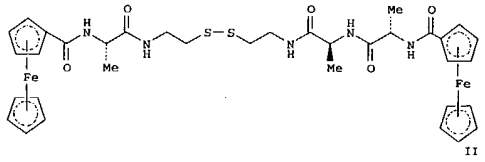


II

AB The syntheses and characterizations of several sym. ferrocenoyl (Fc)-peptide cystamines (CSA), [Fc-Gly-CSA]2, [Fc-Ala-CSA]2, [Fc-Ala-Ala-CSA]2, [Fc-Phe-Ala-CSA]2, I (X = Gly, Ala, Ala-Ala, Phe-Ala, resp.), together with an unsym. Fc-Ala-CSA-Ala-Ala-Fc (II), are reported. All systems show intermol. hydrogen bonding in solution In the solid-state, [Fc-Gly-CSA]2 and [Fc-Ala-CSA]2 exhibit strong intermol. hydrogen bonding, as expected from solution studies, forming a network of β-helical supramol. structures. Monolayers of the Fc-peptide cystamines produced structures that show a uniform thickness of 7(2) Å but are not well ordered, leaving about 10-15% of the Au surface exposed as determined by Cu underpotential deposition. E0' values of all the monolayers are in the range of 460-510 mV. Monolayer dilution with hexanethiol caused an anodic

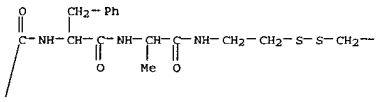
L4 ANSWER 13 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
redox shift of approx. 20 mV and a slight increase in the electron-transfer kinetics.

IT **651019-87-3P**
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); SPN (Synthetic preparation); PREP (Preparation); PROC (Process)
(preparation of disulfide-bonded ferrocenoyl peptides, studies of their solid-state structures, their monolayer assembly on Au surface and electrochem. properties)

RN 651019-87-3 CAPLUS

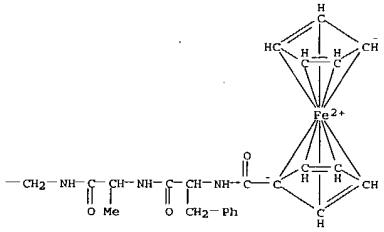
CN L-Alaninamide, 2,2'-(dithiodi-2,1-ethanediyl)bis[N-(ferrocenylcarbonyl)-L-phenylalanyl- (9CI) (CA INDEX NAME)

PAGE 1-A

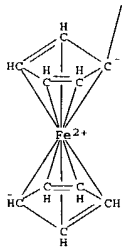


L4 ANSWER 13 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B



PAGE 2-A



REFERENCE COUNT: 94 THERE ARE 94 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:940762 CAPLUS
DOCUMENT NUMBER: 140:216323
TITLE: Quantification of ochratoxin A in foods by a stable isotope dilution assay using high-performance liquid chromatography-tandem mass spectrometry
AUTHOR(S): Lindenmeier, Michael; Schieberle, Peter; Rychlik, Michael
CORPORATE SOURCE: Institut fuer Lebensmittelchemie der Technischen Universitaet Muenchen, Garching, D-85748, Germany
SOURCE: Journal of Chromatography, A (2004), 1023(1), 57-66
CODEN: JCRAEY; ISSN: 0021-9673
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

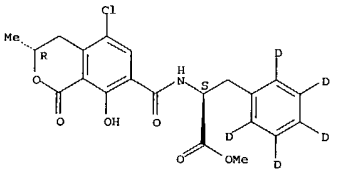
AB A stable isotope dilution assay (SIDA) was developed for quantification of the mycotoxin ochratoxin A (OTA) by using [2H5]-OTA as internal standard The synthesis of labeled OTA was accomplished by acid hydrolysis of unlabeled OTA and subsequent coupling one of the products, ochratoxin α, to [2H5]-L-phenylalanine. The mycotoxin was quantified in foods by LC-tandem MS after extraction with buffers containing [2H5]-OTA and clean-up by immuno affinity chromatog. or by solid phase extraction on silica. The method showed a sufficient sensitivity with a low detection and quantification limit of 0.5 and 1.4 μg/kg, resp., and good precision in inter-assay studies showing a CV (n = 3) of 3.6%. The anal. of certified reference materials resulted in a low bias of 2.1% from the certified values and revealed excellent accuracy of the new method. To prove the suitability of SIDA, OTA was quantified in a number of food samples in which OTA was mostly undetectable. However, three samples of raisins exceeded the legal limit of 10 μg/kg and highlighted the need for further controlling the contamination by the mycotoxin.

IT **666236-26-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(determination of ochratoxin A in food by stable isotope dilution assay using HPLC-tandem mass spectrometry)

RN 666236-26-6 CAPLUS

CN L-Phenyl-d5-alanine, N-[[(3R)-5-chloro-3,4-dihydro-8-hydroxy-3-methyl-1-oxo-1H-2-benzopyran-7-yl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

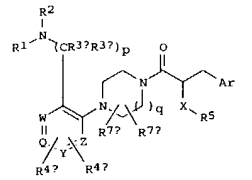
ACCESSION NUMBER: 2003:913002 CAPLUS
DOCUMENT NUMBER: 139:395952
TITLE: Substituted piperazine derivatives as melanocortin receptor ligands, and their preparation, pharmaceutical compositions, and use
INVENTOR(S): Pontillo, Joseph; Marinkovic, Dragan; Lanier, Marion C.; Tran Joe Ahn; Arellano, Melissa; Parker, Jessica; Nelson, Jodie; Chen, Chen; Chen, Caroline; Jiang, Wanglong; White, Nicole; Tucci, Fabio C.
PATENT ASSIGNEE(S): Neurocrine Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 153 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003094918	A1	20031120	WO 2003-US14628	20030509
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004053933	A1	20040318	US 2003-434803	20030509

PRIORITY APPLN. INFO.: US 2002-379517P P 20020510
US 2002-422272P P 20021029

OTHER SOURCE(S): MARPAT 139:395952
GI

L4 ANSWER 15 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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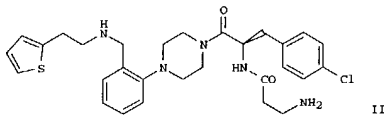


II

AB Compds. are disclosed, which function as melanocortin receptor ligands (no data), and which have utility in the treatment of melanocortin receptor-based disorders. The compds. have structure I [q = 1 or 2; p = 1-3; W, Q, Y, Z = CH or N, provided that ≤ 2 are N, and that when 2 are N, then the N atoms are not adjacent; Ar = (un)substituted Ph or naphthyl; X = bond, O, S, N(R6a), N(R6a)C(O), N(R6a)S(O)2, N(R6a)C(O)N(R6b), C(O)O, OC(O), N(R6a)C(O)N(R6b)O, N(R6a)C(O)N(R6b)N(R6c), or N(R6a)C(O)O; R1, R2, R3a, R3b = H, (un)substituted alkyl, aryl, arylalkyl, heterocyclyl, or heterocyclylalkyl; R4a and R4b = optional ring substituents selected from OH, (un)substituted alkyl, cyano, halo, alkoxy, or alkylamino; R5 = H, (un)substituted alkyl, aryl, or heterocyclyl; R6a, R6b, R6c = H, (un)substituted alkyl; R7a, R7b = optional ring substituents selected from H and (un)substituted alkyl; provided that when p = 1 then R1, R2, R3a, and R3b cannot all be H; including stereoisomers, prodrugs, and pharmaceutically acceptable salts]. Pharmaceutical compns. containing I, as well as methods relating to their use, are also disclosed. Approx. 450 examples of compds. I and salts were prepared, as well as various intermediates. For instance, 1-Cbz-piperazine was N-arylated with 2-fluorobenzaldehyde (53%), followed by reductive amination of the aldehyde with 2-thiopheneethanamine, N-protection of the chain amino as the BOC derivative (82%, 2 steps), hydrogenolysis of CBZ (35%), peptide coupling with D-N-Fmoc-4-chlorophenylalanine using EDC, removal of Fmoc (87%, 2 steps), another peptide coupling with N-BOC-β-alanine, and removal of BOC, to give invention compound II, isolated as the trifluoroacetate salt.

IT **626219-09-8P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

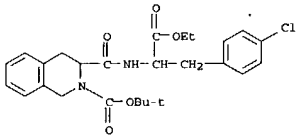
(intermediate; preparation of substituted piperazine derivs. as melanocortin

L4 ANSWER 15 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

receptor liganda)

RN 626219-09-8 CAPLUS

CN 2(1H)-Isoquinolinecarboxylic acid, 3-[[[1-[(4-chlorophenyl)methyl]-2-ethoxy-2-oxoethyl]amino]carbonyl]-3,4-dihydro-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:818297 CAPLUS

DOCUMENT NUMBER: 139:302018

TITLE: Proteasome inhibitors for treating Flaviviridae infections

INVENTOR(S): Schubert, Ulrich; Will, Hans; Sirma, Huseyin

PATENT ASSIGNEE(S): Viromics G.m.b.H., Germany

SOURCE: PCT Int. Appl., 64 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003084551	A1	20031016	WO 2003-DE1213	20030404
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10316735	A1	20031120	DE 2003-10316735	20030404

PRIORITY APPLN. INFO.: DE 2002-10216227 A 20020405

AB The invention discloses agents used in the treatment, therapy and inhibition of Flaviviridae virus infections containing, as active constituents, proteasome inhibitors. The agents, which are used for inhibiting the release, maturation and replication of Flaviviridae, contain, as active components in pharmaceutical prepns., compds. which inhibit the 26S proteasome. The compds.include proteasome inhibitors that influence the activities of the ubiquitin/proteasome pathway, particularly the enzymic activities of the 26S and 20S proteasome complexes. The invention is useful for antiviral therapy of Flaviviridae infections, especially in preventing the establishment and the sustainment of a chronic hepatitis C virus infection and of hepatopathogenesis associated therewith.

IT **179324-59-5**

RL: AGR (Agricultural use); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

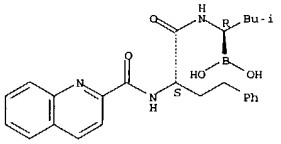
(proteasome inhibitors for treating Flaviviridae infections)

RN 179324-59-5 CAPLUS

CN Boronic acid, [(1R)-3-methyl-1-[[(2S)-1-oxo-4-phenyl-2-[(2-quinolinylcarbonyl)amino]butyl]amino]butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 16 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:788828 CAPLUS
DOCUMENT NUMBER: 140:246179
TITLE: In vitro and in vivo antipseudomonal activity, acute toxicity, and mode of action of a newly synthesized fluoroquinolonyl ampicillin derivative
AUTHOR(S): Lin, Wen-po; Ji, Dar-der; Shiau, Chia-yang; Yang, Tsе-chun; Yang, Yung-wen; Tsou, Tai-li; Tang, Shang-tao; Chen, Chi-hsing; Liu, Yu-tien
CORPORATE SOURCE: Institutes of Microbiology and Immunology, Preventive Medicine and Medical Science, Section of Bacteriology, Division of clinical Pathology, National Defense Medical Center, Tri-Service General Hospital, Taipei, Taiwan
SOURCE: Journal of Laboratory and Clinical Medicine (2003), 142(3), 158-165
CODEN: JLCMAK; ISSN: 0022-2143
PUBLISHER: Mosby, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Compds. N-(6,7-difluoroquinolonyl)-ampicillin (AU-1) and N-(6-fluoroquinolonyl)-ampicillin (FQ-1), synthesized by coupling of the carboxyl group of 6,7-difluoroquinolone (FP-3) and 6-fluoroquinolone (FP4), resp., with the α-amino-group of ampicillin side chain, exhibit antipseudomonal activity similar to and lower acute toxicity than that of norfloxacin, whereas neither ampicillin nor the fluoroquinolone moieties, compound FP-3 or FP4, alone have such activity. Also, AU-1 and FQ-1 are active against tested clin. isolates of Pseudomonas aeruginosa that are highly resistant to norfloxacin, gentamicin, or both. The therapeutic efficacies of FQ-1 and norfloxacin were assessed and compared in neutropenic mice infected with a 90% LD of P aeruginosa. Mice i.p. administered FQ-1 (10 mg/kg) 4, 8, 24, and 48 h after infection had survival rates as high as 80%, comparable to those of mice treated with norfloxacin at the same dosage and dosing schedule. The study of protoplast formation revealed that FQ-1 did not inhibit cell-wall biosynthesis but did induce cell filamentation of Bacillus subtilis at a level close to its minimal inhibition concentration Both AU-1 and FQ-1 were able to intercalate into the double-stranded DNA. However, that FQ-1 lost such activity after it was treated with penicillinase suggests that the lactam-ring structure in ampicillin moiety of FQ-1 was hydrolyzed by penicillinase and that the hydrolyzed structure of FQ-1 does not own DNA-intercalation activity.

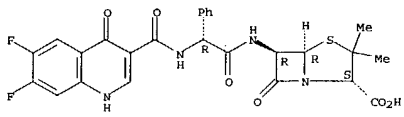
IT **190902-80-8**
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(fluoroquinolonyl ampicillin derivative in vitro and in vivo antipseudomonal activity and acute toxicity and mode of action)

RN 190902-80-8 CAPLUS

CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[(2R)-[[(6,7-difluoro-1,4-dihydro-4-oxo-3-quinolinyl)carbonyl]amino]phenylacetyl]amino]-3,3-dimethyl-7-oxo-, (2S,5R,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 17 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 18 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:746685 CAPLUS
TITLE: Stoichiometric preference in copper-promoted oxidative DNA damage by ochratoxin A. [Erratum to document cited in CA139:392373]
AUTHOR(S): Manderville, Richard A.; Calcutt, M. Wade; Dai, Jian; Park, Gyungse; Gillman, Ivan G.; Noftle, Ronald E.; Mohammed, Abdul K.; Birincioglu, Mustafa; Dizdaroglu, Miral; Rodriguez, Henry; Akman, Steven A.
CORPORATE SOURCE: Department of Chemistry, Wake Forest University, Winston-Salem, NC, 27109-7486, USA
SOURCE: Journal of Inorganic Biochemistry (2003), 97(2), 249
CODEN: JIBIDJ; ISSN: 0162-0134
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal; Errata
LANGUAGE: English

AB An erratum.

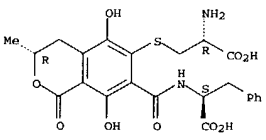
IT INDEXING IN PROGRESS

IT **560134-09-0P**
RL: BSU (Biological study, unclassified); FMU (Formation, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); RACT (Reactant or reagent)
(stoichiometric preference in copper-promoted oxidative DNA damage by ochratoxin A)

RN 560134-09-0 CAPLUS

CN L-Phenylalanine, N-[[(3R)-6-[[(2R)-2-amino-2-carboxyethyl]thio]-3,4-dihydro-5,8-dihydroxy-3-methyl-1-oxo-1H-2-benzopyran-7-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 19 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

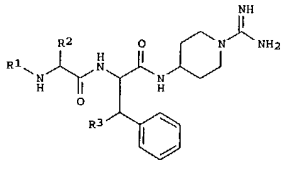
ACCESSION NUMBER: 2003:737774 CAPLUS
DOCUMENT NUMBER: 139:246221
TITLE: Preparation of acylaminopiperidine-1-carboxamidines as inhibitors of plasma kallikrein
INVENTOR(S): Evans, David Michael
PATENT ASSIGNEE(S): Ferring BV, Neth.
SOURCE: PCT Int. Appl., 35 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003076458	A2	20030918	WO 2003-GB908	20030304
WO 2003076458	A3	20031106		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2002-5527 A 20020308
OTHER SOURCE(S): MARPAT 139:246221
GI



I

AB Peptides I [R1 is H, alkyl, R4-CO, R4-O2CCH2, R5-OCO, R5-SO2 (R4 is H, alkyl, Ph and R5 is alkyl, Ph, benzyl); R2 is alkyl, cycloalkyl or cycloalkylalkyl optionally substituted with an alkyl or alkyloxy group, aralkyl optionally substituted with up to three groups chosen from F, Cl, Br, I, OH, alkyl, O-alkyl, O-benzyl, NH2, NO2, NH-acyl, CN, or CF3, or aralkyloxymethyl optionally substituted with up to three groups chosen from F, Cl, Br, OH, alkyl, or O-alkyl; or R1 and R2 together are an o-xylylene group optionally substituted on the aromatic ring by F, Cl, Br, OH, alkyl and O-alkyl; R3 is H, OH, O-alkyl] or pharmaceutically-acceptable salts were prepared as inhibitors of plasma kallikrein. Thus,

L4 ANSWER 19 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

(2'S,2''R)-4-[2'-[2''-amino-3''-(4'''-ethoxyphenyl)propanoylamino]-3'-phenylpropanoylamino]piperidine-1-carboxamidine (I; R1, R3 = H, R2 = p-EtOC6H4CH2, stereo not shown) trifluoroacetate was prepd. via peptide coupling in soln. and showed Ki = 4.5 nM for inhibition of plasma kallikrein.

IT **599201-08-8P**

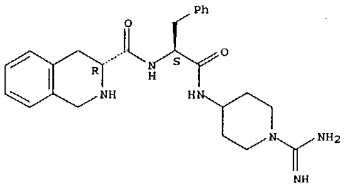
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of peptidyl acylaminopiperidinecarboxamidines as inhibitors of plasma kallikrein)

RN 599201-08-8 CAPLUS

CN 3-Isoquinolinecarboxamide, N-[(1S)-2-[[1-(aminoiminomethyl)-4-piperidinyl]amino]-2-oxo-1-(phenylmethyl)ethyl]-1,2,3,4-tetrahydro-, (3R)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 20 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

CM 2

CRN 64-19-7
CMF C2 H4 O2

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:721766 CAPLUS
DOCUMENT NUMBER: 139:323784
TITLE: Synthesis of 1-(m-hydroxybenzyl)-substituted 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid derivatives as opioid peptide mimetics - unexpected amide bond cleavages under mild conditions
AUTHOR(S): Mannekens, Els; Crisma, Marco; Van Cauwenberghe, Sylvia; Tourwe, Dirk
CORPORATE SOURCE: Laboratorium voor Organische Chemie, Vrije Universiteit Brussel, Brussels, 1050, Belg.
SOURCE: European Journal of Organic Chemistry (2003), (17), 3300-3307
CODEN: EJOCFK; ISSN: 1434-193X
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:323784

AB N-Glycyl-(1R,3S)-1-(m-hydroxybenzyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (Tic) was prepared as a Tyr-Tic dipeptide mimetic for exploration of its potential as a delta opioid receptor selective ligand. The compound was successfully obtained by a stereoselective synthesis starting from L-Tic. In the course of the reactions, unusual peptide bond cleavages were observed under mild conditions, and reaction mechanisms have been proposed.

IT **613232-52-3P**

RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(asym. synthesis of hydroxybenzyl-substituted tetrahydroisoquinoline carboxylic acids as opioid peptidomimetics starting from Tic via stereoselective alkylation)

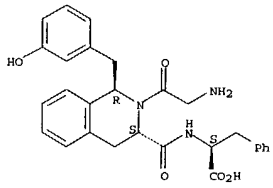
RN 613232-52-3 CAPLUS

CN L-Phenylalanine, glycyl-(1R,3S)-1,2,3,4-tetrahydro-1-[(3-hydroxyphenyl)methyl]-3-isoquinolinecarbonyl-, monoacetate (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 613232-51-2
CMF C28 H29 N3 O5

Absolute stereochemistry.



L4 ANSWER 21 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

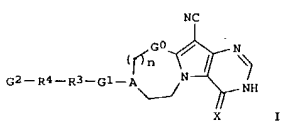
ACCESSION NUMBER: 2003:678812 CAPLUS
DOCUMENT NUMBER: 139:214483
TITLE: Preparation of pyrrolopyrimidine derivatives as GSK-3 inhibitors
INVENTOR(S): Kataoka, Kenichiro; Kosugi, Tomomi; Ishii, Toshihiro; Takeuchi, Takahiro; Tsutsumi, Takaharu; Nakano, Akira; Yamamoto, Yoji; Yoshioka, Noboru
PATENT ASSIGNEE(S): Teijin Limited, Japan
SOURCE: PCT Int. Appl., 210 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003070730	A1	20030828	WO 2003-JP1978	20030224

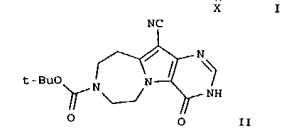
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2002-46129 A 20020222
OTHER SOURCE(S): MARPAT 139:214483
GI



I



II

AB The title pyrrolopyrimidine derivs. with general formula of I [wherein X = O or S; n = 0-2; A = N or CH; G0 = (un)substituted CH2, 2 valence group of (un)substituted benzene, furan, thiophene, pyrrole, isoxazole, cyclopentane, or cyclohexane; G1 = a single bond, CO2, CO, SO2, (un)substituted CONH, CSNH, or CONHSO2; R3 = a single bond,

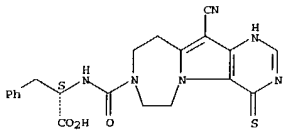
L4 ANSWER 21 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(un)substituted aliph. (cyclo)hydrocarbyl, arom. hydrocarbyl, or heterocyclyl; R4 = a single bond, aliph. cyclohydrocarbyl, arom. hydrocarbyl, or heterocyclyl; G2 = H, CO2H, CONHOH, SO3H, or tetrazol-5-yl] and pharmaceutically acceptable salts thereof are prepd. as glycogen synthetase kinase 3 (GSK-3) inhibitors. For example, the compd. II was prepd. in a multi-step synthesis in good yield. Some of compds. I showed IC50 of <50 nM against GSK-3. I are useful as remedies or preventives for diseases in which GSK-3 participates such as diabetes, diabetic complications, Alzheimer's disease, neurodegenerative disease, depression, traumatic brain injury, hair loss, inflammatory diseases, cancer, immunodeficiency (no data). Formulations contg. I as an active ingredient were also described.

IT **590388-69-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of pyrrolopyrimidine derivs. as GSK-3 inhibitors)

RN 590388-69-5 CAPLUS

CN L-Phenylalanine, N-[(11-cyano-1,4,6,7,9,10-hexahydro-4-thioxo-8H-pyrimido[4',5':4,5]pyrrolo[1,2-d][1,4]diazepin-8-yl)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:665404 CAPLUS

TITLE: Potent and selective cathepsin L inhibitors do not inhibit human osteoclast resorption in vitro. [Erratum to document cited in CA135:120165]

AUTHOR(S): James, Ian E.; Marquis, Robert W.; Blake, Simon M.; Hwang, Shing Mei; Gress, Catherine J.; Ru, Yu; Zembryki, Denise; Yamashita, Dennis S.; McQueney, Michael S.; Tomaszek, Thaddeus A.; Oh, Hye-Ja; Gowen, Maxine; Veber, Daniel F.; Lark, Michael W.

CORPORATE SOURCE: Departments of Bone and Cartilage Biology, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406, USA

SOURCE: Journal of Biological Chemistry (2003), 278(34), 32484
CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal; Errata

LANGUAGE: English

AB An erratum.

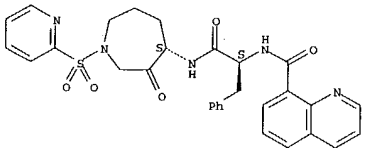
IT INDEXING IN PROGRESS

IT **350796-41-7**
RL: BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(potent and selective cathepsin L inhibitors do not inhibit human osteoclast resorption in vitro (Erratum))

RN 350796-41-7 CAPLUS

CN 8-Quinolinecarboxamide, N-[(1S)-2-[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 23 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:656752 CAPLUS

DOCUMENT NUMBER: 139:197392

TITLE: Preparation of N-carbamoyl nitrogen-containing fused ring compounds as mitochondrial benzodiazepine receptor (MBR) antagonists

INVENTOR(S): Seko, Takuya; Katsumata, Seishi; Kato, Masashi; Manako, Jun-ichiro; Ohmoto, Kazuyuki

PATENT ASSIGNEE(S): Ono Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003068753	A1	20030821	WO 2003-JP1481	20030213

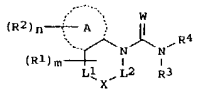
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2002-36340 A 20020214

OTHER SOURCE(S): MARPAT 139:197392

GI



I

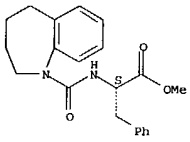
AB The title compds. (I) [wherein the ring A = C5-8 monocyclic carbocyclic ring or 5- to 8-membered monocyclic heterocyclic ring containing 1 or 2 N, 1 or 2 O and/or one S atom; X = CH2, O, S, SO, SO2; L1, L2 = a single bond, C1-4 alkylene, C2-4 alkenylene, provided that a sum total of C atoms in L1 and L2 is 3 or 4; R1 , R2 = each (un)substituted C1-8 alkyl, C2-8 alkenyl, or C2-8 alkynyl, ring B, OR5, NR6R7, COR8, O2CR8, O2CNR6R7, CO2R8, CONR6R7, SR9, SOR8, SO2R8, SO2NR6R7, halo, CO2H, cyano, NO2, oxo, etc.; the ring B = (un)substituted C3-10 monocyclic or dicyclic carbocyclic ring or monocyclic or dicyclic heterocyclic ring containing 1 or 2 N, 1 or 2 O and/or one S atom; R5 = each (un)substituted C1-8 alkyl, C2-8 alkenyl, or C2-8 alkynyl, etc.; R6, R7 = H, -D1-D2 (wherein D1 = a single bond, CO, CO2, or SO2; D2 = each (un)substituted C1-8 alkyl, C2-8 alkenyl, or C2-8 alkynyl, etc.); R8 = groups listed in D2; R9 = each (un)substituted C1-8 alkyl, C2-8 alkenyl, or C2-8 alkynyl, ring B; R3 = H, ring B, each (un)substituted C1-8 alkyl, C2-8 alkenyl, or C2-8 alkynyl; R4 = H, C1-8 alkyl, C2-8 alkenyl, or C2-8 alkynyl; or NR3R4 = (un)substituted 5- to 10-membered monocyclic or dicyclic heterocyclyl containing one N atom and optionally 1-3 N, one O, and/or one S atoms; m, n = an integer of 0-4; W = O, S] were prepd. Also disclosed are mitochondrial benzodiazepine receptor (MBR) antagonists comprising these compds. I and preventives and/or remedies for diseases caused by stress which comprise the above compds. I as the active ingredient. Because of having an MBR antagonistic activity and inhibiting the prodn. of neurosteroids, the compds. I are useful as preventives and/or remedies for diseases caused by stress. The diseases induced, worsened, or exacerbated by stress include digestive organ disease, circulatory system disease, endocrine-metabolic disease, respiratory disease, nerve-muscular disease, skin disease, surgical disease, orthopedic disease, urinary organ-reproductive disease, gynecol. disease (gynopathy), eye disease, otolaryngol. (ear, nose and throat) disease, dental-oral surgical disease, and cancer. The digestive organ disease include functional indigestion, stomach-duodenal ulcer, ulcerative colitis, irritable bowel syndrome, biliary tract dyskinesia, esophagism, gastroatonia (atony of stomach), chronic hepatitis, and chronic pancreatitis. Thus, 250 mg Ph isocyanate was added to a soln. of 560 mg 5-(tert-butyldimethylsilyloxy)-2,3,4,5-tetrahydro-1H-1-benzazepine (prepn. given) in toluene and refluxed overnight to give, after silica gel chromatog., 655 mg 5-(tert-butyldimethylsilyloxy)-1-phenylcarbamoyl-2,3,4,5-tetrahydro-1H-1-benzazepine. The latter compd. (676 mg) was dissolved in 3 mL THF, treated with 2 mL 1 M Bu4NF, and stirred for 5 h to give, after silica gel chromatog., 459 mg 5-hydroxy-1-phenylcarbamoyl-2,3,4,5-tetrahydro-1H-1-benzazepine. 1-(2,6-Dichlorophenylcarbamoyl)-2,3,4,5-tetrahydro-1H-1-benzazepine in vitro inhibited the binding of [3H]PK11195 (MBR-selective ligand) to rat brain membrane sample with Ki of 0.09 nM. A tablet formulation contg. 8-fluoro-5-(4-fluorophenyl)-1-(4-hydroxyphenylcarbamoyl)-2,3,4,5-tetrahydro-1H-1-benzazepine was described.

IT **585576-70-1P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of carbamoyl nitrogen-containing fused ring compds. as mitochondrial benzodiazepine receptor antagonists for treating or preventing diseases caused by stress)

RN 585576-70-1 CAPLUS

CN L-Phenylalanine, N-[(2,3,4,5-tetrahydro-1H-1-benzazepin-1-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

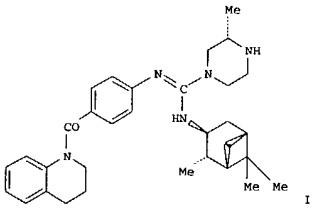
L4 ANSWER 24 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:633668 CAPLUS
DOCUMENT NUMBER: 139:197505
TITLE: Preparation of aryl- or heteroaryl-containing guanidines as melanocortin-4-receptor agonists useful against disorders such as obesity or type II diabetes
INVENTOR(S): Boyce, Rustum; Chu, Daniel
PATENT ASSIGNEE(S): Chiron Corporation, USA
SOURCE: PCT Int. Appl., 102 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003066597	A2	20030814	WO 2003-US1078	20030203
US 2003195187	A1	20031016	US 2003-351574	20030127

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-353188P P 20020204
US 2003-351574 A 20030127
OTHER SOURCE(S): MARPAT 139:197505
GI



I

AB A variety of small, guanidino group-containing mols. (I; A1-A2-A3-A4; A2 = (un)substituted aryl and heteroaryl; A3 is a covalent bond such that A2 is directly bonded to A4, or A3 is a linking group O, S, -NRa-, -C(O)-, -C(O)O-, -NRaC(O)-, -SO2NRa-, -C(S)-, -C(O)S-, -P(O)Rb-, -SO2-, and -S(O)-, wherein if A3 is a linking group, then it is bonded to A2 and A4 in a configuration A2-O-A4, A2-S-A4, A2-NRa-A4, A2-C(O)-A4, A2-C(O)O-A4, A4-C(O)O-A2, A2-NRaC(O)-A4, A4-NRaC(O)-A2, A2-SO2NRa-A4, A4-SO2NRa-A2, A2-C(S)-A4, A2-(C:O)S-A4, A4-(C:O)S-A2, A2-(P:O)Rb-A4, A2-SO2-A4, and A2-S(O)-A4 provided that if A3 is a linking group with the configuration A4-NRaC(O)-A2, then A2 is not a (un)substituted Ph and is not a (un)substituted 6-membered N-contg. heteroaryl. A4 = (un)substituted arylalkyl, heteroarylalkyl, aryl, heteroaryl, heterocyclyl, cycloalkyl, heterocyclylalkyl, cycloalkylalkyl, alkenyl, alkynyl, and alkyl; Ra = H, and (un)substituted arylalkyl, heteroarylalkyl, aryl, heteroaryl, heterocyclyl, cycloalkyl, heterocyclylalkyl, cycloalkylalkyl, alkenyl, alkynyl, and alkyl; Rb = (un)substituted arylalkyl, heteroarylalkyl, aryl, heteroaryl, heterocyclyl, cycloalkyl, heterocyclylalkyl, cycloalkylalkyl, alkenyl, alkynyl, and alkyl.

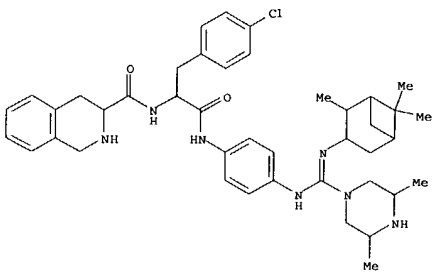
L4 ANSWER 24 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

variables defined below; e.g. (3S)-N'-[4-(3,4-dihydroquinolin-1(2H)-ylcarbonyl)phenyl]-3-methyl-N-[(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]piperazine-1-carboximidamide (shown as I)) capable of acting as MC4-R agonists are provided. The compds. are useful in treating MC4-R mediated diseases and may be formulated into pharmaceutical formulations and compns. Although the methods of prepn. are not claimed, several example prepns. of I and a no. of example prepns. of intermediates are included; 131 addnl. examples of I are tabulated with mass spectral characterization data. Some of the I have -log EC50 values above .apprx.3. Compds. I showed beneficial effects in in vivo studies on energy intake, body wt., hyperinsulinemia, and glucose levels in male 9-10 wk old ob/ob mice that display early onset of obesity, insulin resistance and diabetes due to leptin deficiency. For I: A1 = R1'R2'NC(:NR3')NR4'-, R1'R2'NC(NR3'R4'):N-; R1' = H, and (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, arylalkyl, heteroarylalkyl, and cycloalkylalkyl; R2' = (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, heterocyclyl, arylalkyl, heteroarylalkyl, and cycloalkylalkyl; or R1' and R2', together with the N to which they are bound, form a (un)substituted heterocyclyl or heteroaryl; R3' = (un)substituted aryl, alkyl, alkenyl, alkynyl, cycloalkyl, heteroaryl, heterocyclyl, heterocyclylalkyl, arylalkyl, heteroarylalkyl, and cycloalkylalkyl; R4' = H, and (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclylalkyl, cycloalkylalkyl, aryl, heteroaryl, heterocyclyl, arylalkyl, and heteroarylalkyl. A2 = (un)substituted aryl and heteroaryl; A3 is a covalent bond such that A2 is directly bonded to A4, or A3 is a linking group O, S, -NRa-, -C(O)-, -C(O)O-, -NRaC(O)-, -SO2NRa-, -C(S)-, -C(O)S-, -P(O)Rb-, -SO2-, and -S(O)-, wherein if A3 is a linking group, then it is bonded to A2 and A4 in a configuration A2-O-A4, A2-S-A4, A2-NRa-A4, A2-C(O)-A4, A2-C(O)O-A4, A4-C(O)O-A2, A2-NRaC(O)-A4, A4-NRaC(O)-A2, A2-SO2NRa-A4, A4-SO2NRa-A2, A2-C(S)-A4, A2-(C:O)S-A4, A4-(C:O)S-A2, A2-(P:O)Rb-A4, A2-SO2-A4, and A2-S(O)-A4 provided that if A3 is a linking group with the configuration A4-NRaC(O)-A2, then A2 is not a (un)substituted Ph and is not a (un)substituted 6-membered N-contg. heteroaryl. A4 = (un)substituted arylalkyl, heteroarylalkyl, aryl, heteroaryl, heterocyclyl, cycloalkyl, heterocyclylalkyl, cycloalkylalkyl, alkenyl, alkynyl, and alkyl; Ra = H, and (un)substituted arylalkyl, heteroarylalkyl, aryl, heteroaryl, heterocyclyl, cycloalkyl, heterocyclylalkyl, cycloalkylalkyl, alkenyl, alkynyl, and alkyl; Rb = (un)substituted arylalkyl, heteroarylalkyl, aryl, heteroaryl, heterocyclyl, cycloalkyl, heterocyclylalkyl, cycloalkylalkyl, alkenyl, alkynyl, and alkyl.

IT **582297-17-4P**, (3R)-N-[(1R)-1-[(4-Chlorophenyl)methyl]-2-[[4-[[(Z)-[(3R,5S)-3,5-dimethylpiperazin-1-yl][[(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]imino]methyl]amino]phenyl]amino]-2-oxoethyl]-1,2,3,4-tetrahydroisoquinoline-3-carboxamide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of aryl- or heteroaryl-containing guanidines as melanocortin-4-receptor agonists useful against disorders such as obesity or type II diabetes)

RN 582297-17-4 CAPLUS
CN 3-Isoquinolinecarboxamide, N-[(1R)-1-[(4-chlorophenyl)methyl]-2-[[4-[[(Z)-[(3R,5S)-3,5-dimethyl-1-piperazinyl][[(1S,2S,3S,5R)-2,6,6-trimethylbicyclo[3.1.1]hept-3-yl]imino]methyl]amino]phenyl]amino]-2-oxoethyl]-1,2,3,4-tetrahydro-, (3R)- (9CI) (CA INDEX NAME)

L4 ANSWER 24 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 25 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:610477 CAPLUS
DOCUMENT NUMBER: 139:169275
TITLE: Trojan inhibitors for use in treatment of viral infections
INVENTOR(S): Schubert, Ulrich; Schubert, Evelyn; Tessmer, Uwe; Lucas, Kerstin
PATENT ASSIGNEE(S): Viromics G.m.b.H., Germany
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003064453	A2	20030807	WO 2003-DE265	20030127
WO 2003064453	A3	20040212		
DE 10304202	A1	20031204	DE 2003-10304202	20030127

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: DE 2002-10203862 A 20020127
DE 2002-10204210 A 20020127
DE 2002-10209064 A 20020228

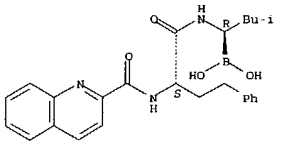
AB The invention relates to active inhibitors - Trojan inhibitors (TI) - and the use thereof in the form of specifically shaped Trojan proteasome-inhibitors (TPI) or Trojan assembling-inhibitors (TAI), such as proteasome-and assembling-inhibitors which are, initially, inactive and are only activated in the target cell by means of a protease specific for the target cell. According to the invention, said inhibitor can be used in the treatment of viral infections, whereby a virus-specific protease is expressed, particularly in HIV-infections and AIDS-therapy, and optionally in the inhibition of the release, maturing and replication of filo viruses, and in the treatment and prevention of viral haemorrhagic fever (activated by Ebola or Marburg-viruses) and in the therapy of tumoral diseases, whereby the tumor cells are characterised by a specific protease.

IT **179324-59-5**, PS 325
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Trojan inhibitors for use in treatment of viral infections)

RN 179324-59-5 CAPLUS
CN Boronic acid, [(1R)-3-methyl-1-[[(2S)-1-oxo-4-phenyl-2-[(2-quinolinylcarbonyl]amino]butyl]amino]butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 25 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 26 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:591206 CAPLUS
DOCUMENT NUMBER: 139:145837
TITLE: Substrates for monitoring Staphylococcus aureus cysteine peptidase activity and use for screening antibacterial agents
INVENTOR(S): Ramjee, Manoj Kumar
PATENT ASSIGNEE(S): Amura Therapeutics Limited, UK
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003062267	A2	20030731	WO 2003-GB120	20030116
WO 2003062267	A3	20030904		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 2002-1040 A 20020117
GB 2002-16508 A 20020716
OTHER SOURCE(S): MARPAT 139:145837

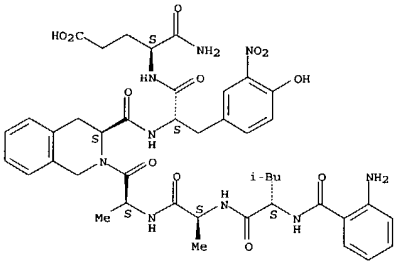
AB The invention provides peptide substrayes for monitoring Staphylococcus aureus cysteine peptidase activity and use for screening antibacterial agents. Compds. of general formula (I): (A) A compound of general formula (I) Y-AA1-AA2-AA3-AA4-R-Glu-NH2, Y-A1-A2-A3-A4-R-Glu-NH2 wherein Y and R are reporter groups; A1 is either the D-isomer or the L-isomer form of isoleucine; each of A2 and A3 is independently Ala or 2-aminobutyric acid (Abu); A4 is Pro, L-3-hydroxyproline (Pro(3-OH)), L-4-hydroxyproline (Pro (4-OH)), L-tetrahydroisoquinoline-1-carboxylic acid (THIQ), L-tetrahydroisoquinoline-3-carboxylic acid (Tic), L-pipecolic acid (Pip), 1-amino-1-cyclopentane carboxylic acid (1-ACP) or D-Pro; and any one of A1, A2, A3 and A4 can be replaced by any other amino acid group (Xaa); and the other protein based substrates are cleavable by Staphyococcus sp. extracellular cysteine protease and are therefore likely to be of use in monitoring enzyme activity for purposes such as investigating candidate enzyme modulators and screening for therapeutic agents.

IT **572919-07-4**
RL: ARG (Analytical reagent use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(substrate sequence; substrates for monitoring Staphylococcus aureus cysteine peptidase activity and use for screening antibacterial agents)

RN 572919-07-4 CAPLUS
CN L-α-Glutamine, N-(2-aminobenzoyl)-L-leucyl-L-alanyl-L-alanyl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-3-nitro-L-tyrosyl- (9CI) (CA INDEX NAME)

L4 ANSWER 26 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.



L4 ANSWER 27 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:591007 CAPLUS
DOCUMENT NUMBER: 139:149922
TITLE: Preparation of piperazinyl amino acid derivatives as melanocortin receptor agonists
INVENTOR(S): Backer, Ryan Thomas; Collado Cano, Ivan; De Frutos-Garcia, Oscar; Doecke, Christopher William; Fisher, Matthew Joseph; Kuklish, Steven Lee; Mancuso, Vincent; Martinelli, Michael John; Mullaney, Jeffrey Thomas; Ornstein, Paul Leslie; Xie, Chaoyu
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003061660	A1	20030731	WO 2003-US33	20030121

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-351200P P 20020123
OTHER SOURCE(S): CASREACT 139:149922; MARPAT 139:149922
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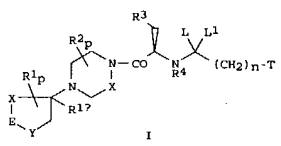


I

AB The invention relates to melanocortin receptor (MC-R) agonists I [LL1 = H2 or oxo; E = O, S, NR1b, SO, SO2, CR9, CR92, where R1b = H, alkyl, alkylsulfonyl, etc. and R9 = H, alk(en)(yn)yl, alkanoyl, Ph, (hetero)aryl; or R9 may combine with adjacent R1 to form a carbocycle; X = CH2 or CH2CH2; Y = (CH2)0-2; the ring containing E may have a double bond; T = substituted (tetrahydro)isoquinolinyl, dihydroisoindolinyl, or piperazinyl; n = 0-8; R1 = H, alkyl, (D)cycloalkyl, aryl, carbalkoxy, etc.; R1a = H, (cyclo)alkyl, (D)(hetero)aryl, aminoalkyl, etc.; R2 = H, alkyl, alkylcarbamoyl, (D)phenyl, (D)cycloalkyl, or oxo adjacent to N attached to the ring containing E; p = 0-4; R3 = (un)substituted Ph, aryl, or thienyl; R4 = H, alkyl, alkoxyalkyl, alkanoyl, or carbalkoxyl or their

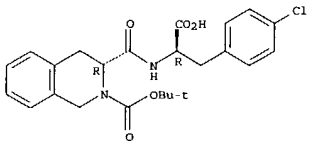
L4 ANSWER 27 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
pharmaceutically-acceptable salts or stereoisomers, which are useful in the treatment of obesity, diabetes, and male and/or female sexual dysfunction. Compds. I comprise three domains, i.e., a piperazinyl fragment, an amino acid, and a radical CLL1(CH2)n-T. Thus, N-[1-[4-chlorobenzyl)-2-[4-(4-isobutyl-1-isopropylpiperidin-4-yl)piperazin-1-yl]-2-oxoethyl]-2-(2,3-dihydro-1H-isoindol-1-yl)acetamide TFA salt was prepd. via acylation of the piperazine moiety and assayed for treatment of sexual dysfunction in rat models (MC4 Ki = 9 nM, MC4 EC50 = 4.2 nM).

IT **252008-71-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperazinyl amino acid derivs. as melanocortin receptor agonists)

RN 252008-71-2 CAPLUS

CN 2(1H)-Isoquinolinecarboxylic acid, 3-[[[(1R)-1-carboxy-2-(4-chlorophenyl)ethyl]amino]carbonyl]-3,4-dihydro-, 2-(1,1-dimethylethyl) ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 28 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2003:590812 CAPLUS
DOCUMENT NUMBER:	139:133836
TITLE:	Preparation of 4-aminoazepan-3-ones as protease inhibitors
INVENTOR(S):	Marquis, Robert Wells; Ru, Yu; Veber, Daniel Frank; Cummings, Maxwell David; Thompson, Scott Kevin; Yamashita, Dennis Shinji
PATENT ASSIGNEE(S):	Smithkline Beecham Corporation, USA
SOURCE:	U.S. Pat. Appl. Publ., 126 pp., Cont.-in-part of U.S. Ser. No. 593,845, abandoned. CODEN: USXXCO
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003144175	A1	20030731	US 2001-881334	20010614
WO 2000038687	A1	20000706	WO 1999-US30730	19991221
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1384713	A1	20040128	EP 2003-76211	19991221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY				
ZA 2001004208	A	20020523	ZA 2001-4208	20010523
WO 2002017924	A1	20020307	WO 2001-US27178	20010831
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001086983	A5	20020313	AU 2001-86983	20010831
EP 1320370	A1	20030625	EP 2001-966474	20010831
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004509083	T2	20040325	JP 2002-522897	20010831
US 2004002487	A1	20040101	US 2003-404716	20030401

PRIORITY APPLN. INFO.:
US 1998-113636P P 19981223
US 1999-164581P P 19991110
WO 1999-US30730 A2 19991221
US 2000-593845 B2 20000614
EP 1999-963112 A3 19991221
US 2000-653815 A2 20000901
US 2001-881334 A2 20010614
WO 2001-US27178 W 20010831

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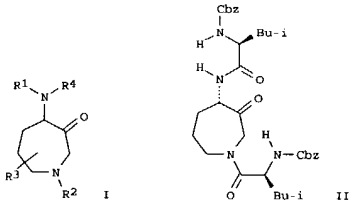
L4 ANSWER 28 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



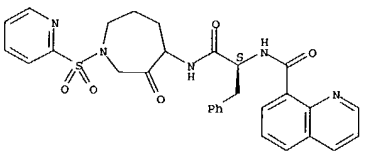
AB Aminoazepanones I [R1 = alkanoyl, amino-, alkoxy-, or alkylthioalkanoyl, etc.; R2 = H, alkyl, cycloalkyl, cycloalkylalkyl, (thio)acyl, alkylsulfonyl, etc.; R3 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, etc.; R4 = H, alkyl, arylalkyl, etc.] or their pharmaceutically-acceptable salts were prepared as protease inhibitors, including cathepsin K, for treating diseases of excessive bone loss or cartilage or matrix degradation, gingival disease, arthritis, Paget's disease, hypercalcemia of malignancy, and metabolic bone disease. Thus, compound II (Cbz = benzyloxycarbonyl) was prepared by a multistep procedure.

IT **281217-12-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (acylamino)azepanones as protease inhibitors)

RN 281217-12-7 CAPLUS

CN 8-Quinolinecarboxamide, N-[(1S)-2-[[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 29 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER:	2003:509842 CAPLUS
DOCUMENT NUMBER:	140:218058
TITLE:	Solid supported parallel synthesis of dimer libraries
AUTHOR(S):	Subra, Gilles; Amblard, Muriel; Durand, Philippe; Komesli, Sylvianne; Renaut, Patrice; Martinez, Jean
CORPORATE SOURCE:	Laboratoire des Aminoacides, Peptides et Proteines, Faculte de Pharmacie, UMR 5810, Montpellier, 34060, Fr.
SOURCE:	Peptides 2000, Proceedings of the European Peptide Symposium, 26th, Montpellier, France, Sept. 10-15, 2000 (2001), Meeting Date 2000, 973-974. Editor(s): Martinez, Jean; Fehrentz, Jean-Alain. Editions EDK: Paris, Fr. CODEN: 69EDWK; ISBN: 2-84254-048-4
DOCUMENT TYPE:	Conference
LANGUAGE:	English

AB A symposium report. Dimer libraries, particularly the JMV 1783 dimer library, were synthesized using lysine as a central template via the Multipin technol. The core of the compds. in the dimer library synthesis is a diamino acid template which is linked to the Synphase crown by a Rink amide type linker. Eleven libraries generated a family of 650 members, of which 10 showed a growth hormone binding inhibition of > 80% at 10-5 M.

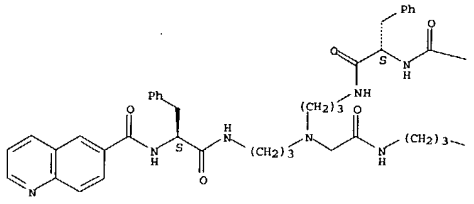
IT **664335-91-5P**, JMV 1946
RL: CPN (Combinatorial preparation); CMBI (Combinatorial study); PREP (Preparation)
(solid supported parallel synthesis of peptide dimer libraries and their growth factor hormone agonist activity)

RN 664335-91-5 CAPLUS

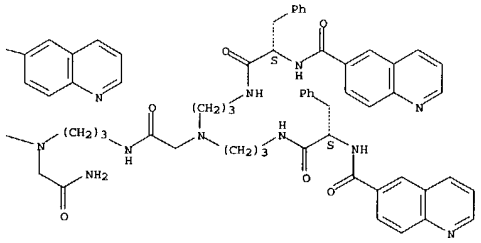
CN 6-Quinolinecarboxamide, N,N',N'',N'''-[[(2-amino-2-oxoethyl)imino]bis[3,1-propanediylimino(2-oxo-2,1-ethanediyl)nitrilobis[3,1-propanediylimino[(1S)-2-oxo-1-(phenylmethyl)-2,1-ethanediyl]]]]tetrakis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



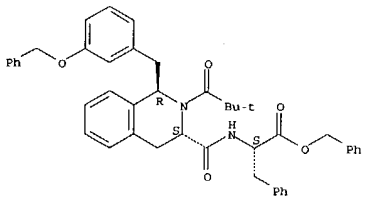
L4 ANSWER 29 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 30 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:509769 CAPLUS
DOCUMENT NUMBER: 140:164185
TITLE: Amide bond cleavages under unusual mild conditions in N-pivaloyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (N-pivaloyl-Tic) compounds: A mechanistic study
AUTHOR(S): Mannekens, Els; Tourwe, Dirk; Crisma, Marco
CORPORATE SOURCE: Laboratorium voor Organische Chemie, Vrije Universiteit Brussel, Brussels, B-1050, Belg.
SOURCE: Peptides 2000, Proceedings of the European Peptide Symposium, 26th, Montpellier, France, Sept. 10-15, 2000 (2001), Meeting Date 2000, 827-828. Editor(s): Martinez, Jean; Fehrentz, Jean-Alain. Editions EDK: Paris, Fr.
CODEN: 69EDWK; ISBN: 2-84254-048-4
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A symposium report. A mechanistic study has been conducted for two cases of amide cleavages during the deprotection of the N-pivaloyl protecting group of 1-[3-(benzyloxy)benzyl]-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid derivs. Mechanisms are proposed for cleavage of the pivaloyl-Tic amide bond and the Tic-Phe amide bond.
IT **613232-44-3**
RL: RCT (Reactant); RACT (Reactant or reagent)
(mechanism of amide bond cleavage of pivaloyltetrahydroisoquinolinecarboxylic acid compds.)
RN 613232-44-3 CAPLUS
CN L-Phenylalanine, N-[[(1R,3S)-2-(2,2-dimethyl-1-oxopropyl)-1,2,3,4-tetrahydro-1-[[3-(phenylmethoxy)phenyl]methyl]-3-isoquinolinyl]carbonyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

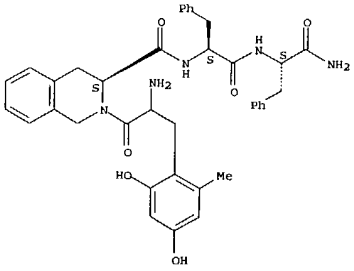
Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 31 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:509722 CAPLUS
DOCUMENT NUMBER: 140:193456
TITLE: Opioid activity profiles of TIPP-related peptides containing 2'-hydroxy,6'-methyltyrosine (Hmt) in place of Tyr
AUTHOR(S): Schiller, Peter W.; Berezowska, Irena; Weltrowska, Grazyna; Lemieux, Carole; Chung, Nga N.
CORPORATE SOURCE: Laboratory of Chemical Biology and Peptide Research, Clinical Research Institute of Montreal, Montreal, QC, H2W 1R7, Can.
SOURCE: Peptides 2000, Proceedings of the European Peptide Symposium, 26th, Montpellier, France, Sept. 10-15, 2000 (2001), Meeting Date 2000, 731-732. Editor(s): Martinez, Jean; Fehrentz, Jean-Alain. Editions EDK: Paris, Fr.
CODEN: 69EDWK; ISBN: 2-84254-048-4
DOCUMENT TYPE: Conference
LANGUAGE: English
AB Syntheses and in vitro opioid activity profiles of the Hmt1-analogs of TIPP-related peptides were presented. Results indicate that Hmt1-analogs of TIPP-related peptides may have unexpected opioid activity profiles, possibly due to the hydrogen bonding capability of the 2'-OH group of Hmt.
IT **660850-07-7**
RL: BSU (Biological study, unclassified); PKT (Pharmacokinetics); PRP (Properties); BIOL (Biological study)
(opioid activity profiles of TIPP-related peptides containing 2'-hydroxy,6'-methyltyrosine (Hmt) in place of Tyr1)
RN 660850-07-7 CAPLUS
CN L-Phenylalaninamide, 2-hydroxy-6-methyltyrosyl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



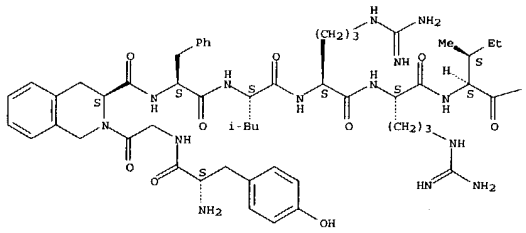
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 32 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:509658 CAPLUS
DOCUMENT NUMBER: 140:157610
TITLE: A structure-activity study of dynorphin(1-13)-peptide amides. Synthesis of analogs with unusual amino acids in positions 0, 2, 3, 4
AUTHOR(S): Bobrova, Irina; Goodman, Murray; DeHaven, Robert N.; Daubert, Jeffrey D.; Johansson, LarsErik; Neumuller, Magnus; Terenius, Lars
CORPORATE SOURCE: Institute of Organic Synthesis, Riga, LV-1006, Latvia
SOURCE: Peptides 2000, Proceedings of the European Peptide Symposium, 26th, Montpellier, France, Sept. 10-15, 2000 (2001), Meeting Date 2000, 603-604. Editor(s): Martinez, Jean; Fehrentz, Jean-Alain. Editions EDK: Paris, Fr.
CODEN: 69EDWK; ISBN: 2-84254-048-4
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A series of dynorphin analogs was synthesized by solid-phase methodol. using Fmoc-amino acid pentafluorophenyl esters. The analogs were synthesized with the following modifications: the amino acid residue at position 2 was replaced by amino acids Phe, cPrAla (β-cyclopropyl-Ala), Tic(tetrahydroisoquinoline), Oic (octahydroindole-2-carboxylic acid), NaI2 (2-naphthylalanine); N-terminal extension with lys0; 3 Gly3 was substituted with cPrAla,Tic; exchange of Phe4 for Tic; and Gly2-Gly3 was replaced by cPrAla-Phe, Tic-Phe, Oic-Phe and NaI2-Phe in analogs with double replacement. The new dynorphin analogs were κ-selective. All of them retained modest μ activity and were essentially inactive at the δ opioid receptor. The presence of cPrAla in position 3 resulted in a compound with the highest κ-activity. Double substitution of Gly-Gly by Tic-Phe afforded an analog which exhibited modest δ-activity.
IT **656256-53-0**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(structure-activity study of dynorphin(1-13)-peptide analogs with unusual amino acids in positions 0, 2, 3, 4)
RN 656256-53-0 CAPLUS
CN 1-13-Dynorphin A (swine), 3-[(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid]-13-L-lysinamide- (9CI) (CA INDEX NAME)

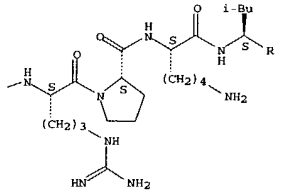
Absolute stereochemistry.

L4 ANSWER 32 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

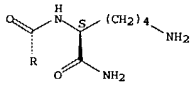
PAGE 1-A



PAGE 1-B



PAGE 2-A



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

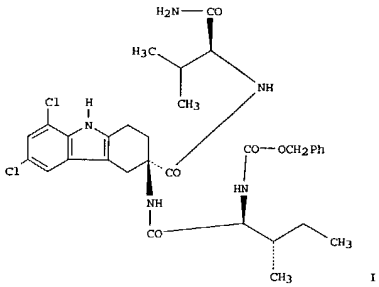
L4 ANSWER 33 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:491183 CAPLUS
DOCUMENT NUMBER: 139:69525
TITLE: Synthesis of tetrahydrocarbazole derivatives for use as ligands for G-protein coupled receptors and antagonists of gonadotropin-releasing hormone for treatment of disease
INVENTOR(S): Koppitz, Marcus; Muhn, Hans Peter; Shaw, Ken; Hess-Stumpp, Holger; Paulini, Klaus
PATENT ASSIGNEE(S): Zentaris Ag, Germany
SOURCE: PCT Int. Appl., 114 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003051837	A2	20030626	WO 2002-EP14344	20021216
WO 2003051837	A3	20040226		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10164564	A1	20030626	DE 2001-10164564	20011214
US 2003232873	A1	20031218	US 2002-319833	20021216
PRIORITY APPLN. INFO.:			DE 2001-10164564 A	20011214
			US 2001-341878P P	20011221
OTHER SOURCE(S):	MARPAT 139:69525			

GI

L4 ANSWER 33 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



I

AB The invention relates to novel tetrahydrocarbazole derivs. [e.g., (I)] which act as ligands for G-protein coupled receptors (GPCR), especially as antagonists of gonadotropin-releasing hormone (GnRH), and pharmaceutical composition containing them. Furthermore, the invention relates to the administration of tetrahydrocarbazole derivs. for the treatment of pathol. conditions mediated by GPCR, especially for the inhibition of GnRH, to mammals, especially humans, requiring such treatment, and to the use of tetrahydrocarbazole derivs. for producing a pharmaceutical agent for treating pathol. conditions mediated by GPCR, especially for the inhibition of GnRH. Limited syntheis of intermediate materials is given, with many tables of products exemplified by general synthesis steps. Thus, beginning from 4,4-ethylenedioxycyclohexanone and phenylhydrazine, I was prepared in seven generalized steps. In in vitro tests with alpha T3-1 cells, I had IC50 for human GnRH of 1.5 x 10-8 M, with Ca2+ release of 4.5 x 10-8 M.

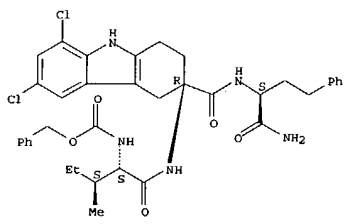
IT **548754-89-8P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tetrahydrocarbazole derivs. for use as ligands for G-protein coupled receptors and antagonists of gonadotropin-releasing hormone for treatment of disease)

RN 548754-89-8 CAPLUS

CN Carbamic acid, [(1S,2S)-1-[[[(3R)-3-[[[(1S)-1-(aminocarbonyl)-3-phenylpropyl]amino]carbonyl]-6,8-dichloro-2,3,4,9-tetrahydro-1H-carbazol-3-yl]amino]carbonyl]-2-methylbutyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 33 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



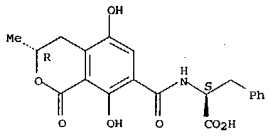
L4 ANSWER 34 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:459828 CAPLUS
DOCUMENT NUMBER: 139:175029
TITLE: Binding of Ochratoxin A Derivatives to Human Serum Albumin
AUTHOR(S): Perry, Jennifer L.; Il'ichev, Yuri V.; Kempf, Valerie R.; McClendon, Jamal; Park, Gyungse; Manderville, Richard A.; Rueker, Florian; Dockal, Michael; Simon, John D.
CORPORATE SOURCE: Department of Chemistry, Duke University, Durham, NC, 27708, USA
SOURCE: Journal of Physical Chemistry B (2003), 107(27), 6644-6647
CODEN: JPCBFK; ISSN: 1520-6106
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ochratoxins are fungal metabolites known to contaminate human and animal feed. Ochratoxin A (OTA) is the most widespread form of the toxins and is believed to be responsible for human renal diseases. For the majority of its lifetime within the body, OTA remains bound to the plasma protein human serum albumin (HSA). In this paper, the binding of three OTA derivs. (ochratoxin B (OTB), ochratoxin hydroquinone (OHQ), and O-methylated OTA (MOA)) to HSA is examined using optical spectroscopy. The binding consts. decrease as follows: OTA2- (5.2+106 M-1) > OTB2- (1.8+106 M-1) > OHQ2- .apprx. OHQ- (2.2+105 M-1) > MOA- (3+104 M-1). Studies of the binding of OTB, OHQ, and MOA to recombinant proteins corresponding to the domains of HSA reveal binding to all domains but with different affinities. Similar to OTA, all derivs. exhibit the largest binding constant for domain 2. These ligands are displaced by 2,3,5-triiodobenzoate (TIB), indicating they share a common binding site and bind to Sudlow Site I within domain 2 of HSA. Derivs. with ionizable phenolic protons exhibit a decreased pKa by as much as two units upon interaction with HSA. The magnitude of the change in pKa observed upon binding decreases in the order OTA > OTB > OHQ. These data suggest a model in which the monoanions of OTA, OTB, and OHQ undergo deprotonation by an arginine within domain 2 upon binding to HSA. The difference in binding constant for the three dianions studied results from the stabilization of the dianion by the surrounding protein matrix.

IT **205034-32-8D**, serum albumin complexes
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(binding of ochratoxin A derivs. to human serum albumin)
RN 205034-32-8 CAPLUS
CN L-Phenylalanine, N-[[(3R)-3,4-dihydro-5,8-dihydroxy-3-methyl-1-oxo-1H-2-benzopyran-7-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 34 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



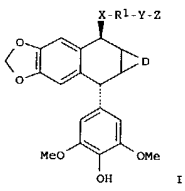
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 35 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:390845 CAPLUS
DOCUMENT NUMBER: 138:385216
TITLE: Preparation of etoposide amino acid analogs as DNA topoisomerase II inhibitors
INVENTOR(S): Lee, Kuo-Hsiung; Xiao, Zhiyan; Bastow, Kenneth F.
PATENT ASSIGNEE(S): The University of North Carolina At Chapel Hill, USA
SOURCE: U.S., 17 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6566393	B1	20030520	US 2002-177147	20020621
US 2004006126	A1	20040108	US 2003-349351	20030122
WO 2004000859	A2	20031231	WO 2003-US19629	20030620

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-177147 A1 20020621
US 2003-349351 A 20030122
OTHER SOURCE(S): MARPAT 138:385216
GI



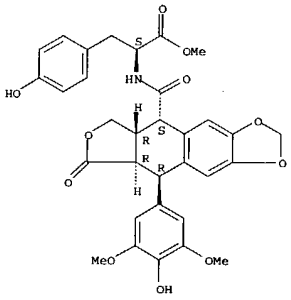
I

AB Etoposide amino acid analogs I (X = O, S, NH, CO, CH:N, CH2NH; R1 = covalent linkage between X and Y, alkyl, alkenyl, (un)substituted Ph; Y = NHCO, CONH; Z = CHR2(CH2)nR3, R2 = CO2H, NH2, ester, etc., R3 = alkyl, alkenyl, aryl, n= 0-2; D = CH2OC(O), CH2OC(:CH2), CH2CH2C(O), CH2OCH2, CH2OC(S), CH2O(SO2)OCH2, etc.) were prepared as DNA topoisomerase II inhibitors. Thus, 4'-O-demethyl-4β-[4''-(methyl-L-tyrosine-N-carbonyl)anilino]-4-desoxy-podophyllotoxin (II) and 4'-O-demethyl-4β-[4''-(methyl-L-tryptophan-N-carbonyl)anilino]-4-desoxypodophyllotoxin were prepd. from podophyllotoxin and their pharmaceutical activity evaluated. The antitumor ED50 of II against A 549 human cell line was 2.4 μM.

L4 ANSWER 35 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

IT **527678-17-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of etoposide amino acid analogs as DNA topoisomerase II inhibitors)
RN 527678-17-7 CAPLUS
CN L-Tyrosine, N-[[(5S,5aR,8aR,9R)-5,5a,6,8,8a,9-hexahydro-9-(4-hydroxy-3,5-dimethoxyphenyl)-8-oxofuro[3',4':6,7]naphtho[2,3-d]-1,3-dioxol-5-yl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 36 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:389448 CAPLUS
DOCUMENT NUMBER: 139:392373
TITLE: Stoichiometric preference in copper-promoted oxidative DNA damage by ochratoxin A
AUTHOR(S): Manderville, Richard A.; Wade Calcutt, M.; Dai, Jian; Park, Gyungse; Gillman, Ivan G.; Noftle, Ronald E.; Mohammed, Abdul K.; Dizdaroglu, Miral; Rodriguez, Henry; Akman, Steven A.
CORPORATE SOURCE: Department of Chemistry, Wake Forest University, Winston-Salem, NC, 27109-7486, USA
SOURCE: Journal of Inorganic Biochemistry (2003), 95(2-3), 87-96
CODEN: JIBIDJ; ISSN: 0162-0134
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

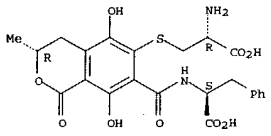
AB The ability of the fungal carcinogen, ochratoxin A (OTA, 1), to facilitate copper-promoted oxidative DNA damage has been assessed using supercoiled plasmid DNA (Form I)-agarose gel electrophoresis and gas chromatog.-mass spectrometry with selected-ion monitoring (GC-MS-SIM). OTA is shown to promote oxidative cleavage of Form I DNA with optimal cleavage efficiency occurring under excess Cu(II) conditions. As the concentration of OTA was increased and present in excess of Cu(II) the cleavage was less effective. Parallel findings were found for the ability of the OTA-Cu mixture to facilitate oxidative base damage. Yields (lesions per 106 DNA bases) of modified bases upon exposure of calf-thymus DNA (CT-DNA) to OTA-H2O2-Cu(II) were diminished when the OTA:Cu ratio was increased to 5:1. Electrochem. studies carried out in methanol implicate a ligand-centered 2e oxidation of OTA in the presence of excess Cu(II), while product analyses utilizing electrospray mass spectrometry support the intermediacy of the quinone, OTQ (3), in Cu-promoted oxidation of OTA. The implications of these findings with regard to the mutagenicity of OTA are discussed.

IT **560134-09-0P**
RL: BSU (Biological study, unclassified); FMU (Formation, unclassified); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); RACT (Reactant or reagent)
(stoichiometric preference in copper-promoted oxidative DNA damage by ochratoxin A)

RN 560134-09-0 CAPLUS
CN L-Phenylalanine, N-[[(3R)-6-[[(2R)-2-amino-2-carboxyethyl]thio]-3,4-dihydro-5,8-dihydroxy-3-methyl-1-oxo-1H-2-benzopyran-7-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 36 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

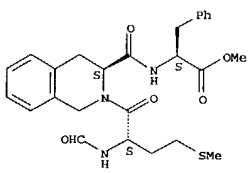
L4 ANSWER 37 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:341041 CAPLUS
DOCUMENT NUMBER: 139:363489
TITLE: Structure-biological response relationship of fMLP analogs in human neutrophils
AUTHOR(S): Spisani, S.; Turchetti, M.; Cavicchioni, G.
CORPORATE SOURCE: Dipartimento di Biochimica e Biologia Molecolare, Universita degli Studi di Ferrara, Ferrara, 44100, Italy
SOURCE: Chemotaxis and Migration (2002), 3(4), 68-83
CODEN: CMHICX; ISSN: 1608-2265
PUBLISHER: VICER Publishing
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Neutrophils constitute the first line of defense against bacterial invasion. They migrate to infected tissues along a concentration gradient of chemoattractant mols., the most important of which is for-Met-Leu-Phe-OH. Different responses arise from binding of formylpeptide with different isoforms of the specific receptor. The goal of studies reported herein was to clarify (i) the role of for-Met-Leu-Phe amide bonds in receptor-ligand crosslinking, (ii) the features peculiar to the Met, Leu, and Phe receptor pockets. The data show: (1) the amide bond at position 2 must be protic, while the amide bond at position 3 participates and links the receptor, but its role is not mandatory. Furthermore, the isoform that elicits chemotaxis is structurally more exacting than the isoform that elicits superoxide anion production; (2) the Met receptor pocket shows a pos. charged area narrow in dimension, located at a well defined distance from the backbone, and oriented in a specific position, not completely surrounding the internally located side chain; (3) the Leu receptor pocket highlights that the hydrophobicity of the second residue is the mandatory key to stimulate a good chemotaxis, while hydrophilicity associated to good steric hindrance elicits a potent superoxide anion production; (4) the features peculiar to the Phe receptor pocket, unexpectedly, prove to be less mandatory in the isoform that elicits chemotaxis, which is strongly stimulated, than in the isoform that triggers superoxide anion production, which instead is less triggered.

IT **177656-62-1**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(structure-biol. response relationship of fMLP analogs in human neutrophils)

RN 177656-62-1 CAPLUS
CN L-Phenylalanine, N-[[(3S)-2-[(2S)-2-(formylamino)-4-(methylthio)-1-oxobutyl]-1,2,3,4-tetrahydro-3-isoquinolinyl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



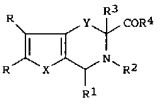
L4 ANSWER 37 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 38 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:319899 CAPLUS
DOCUMENT NUMBER: 138:338490
TITLE: Preparation of β-carboline derivatives as protein tyrosine phosphatase (PTP)-inhibitors
INVENTOR(S): Mjalli, Adnan M. M.; Andrews, Robert C.; Xie, Rongyuan; Yarragunta, Ravindra R.; Ren, Tan
PATENT ASSIGNEE(S): Transtech Pharma, Inc., USA
SOURCE: PCT Int. Appl., 110 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003033496	A1	20030424	WO 2002-US33520	20021018
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004014778	A1	20040122	US 2002-274546	20021018

PRIORITY APPLN. INFO.: US 2001-346125P P 20011019
US 2001-346176P P 20011019
OTHER SOURCE(S): MARPAT 138:338490
GI

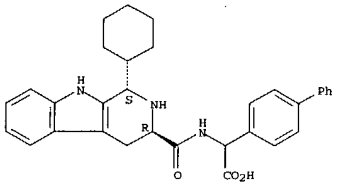


I

AB The invention provides compds. I [RCH:CHR is (un)substituted (hetero)aryl; X is O, S, imino; Y is CH2, CH2CH2; R1 is alk(en)(yn)yl, (hetero)aryl, heterocyclyl, cycloalkyl, (hetero)aryl, etc.; R2 is H, alk(en)(yn)yl, (hetero)aryl, heterocyclyl, cycloalkyl, arylalk(en)(yn)yl, carboxy, etc.; R3 is H, alk(en)(yn)yl, (hetero)arylalk(en)(yn)yl; R4 is OH, (cyclo)alkoxy, (un)substituted amino, etc.] which are useful as inhibitors of protein tyrosine phosphatases (PTPases). Thus, N-benzyl-1-(1,1'-biphenyl-4-yl)-1,2,3,4-tetrahydro-β-carboline-3-carboxamide was prepared from DL-tryptophan Me ester, 4-biphenylcarboxaldehyde, and

L4 ANSWER 38 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
benzylamine.
IT **515157-61-6P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of β-carboline derivs. as protein tyrosine phosphatase (PTP)-inhibitors)
RN 515157-61-6 CAPLUS
CN [1,1'-Biphenyl]-4-acetic acid, α-[[[(1S,3R)-1-cyclohexyl-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-3-yl]carbonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

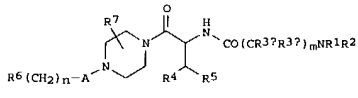


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 39 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:301053 CAPLUS
DOCUMENT NUMBER: 138:321578
TITLE: Preparation of peptides as ligands of melanocortin receptors
INVENTOR(S): Dyck, Brian P.; Goodfellow, Val; Phillips, Teresa; Parker, Jessica; Zhang, Xiaohu; Chen, Chen; Tran, Joe Anh; Pontillo, Joseph; Tucci, Fabio C.
PATENT ASSIGNEE(S): Neurocrine Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 112 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003031410	A1	20030417	WO 2002-US32282	20021009
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003158209	A1	20030821	US 2002-268923	20021009

PRIORITY APPLN. INFO.: US 2001-328295P P 20011009
US 2002-366745P P 20020322
OTHER SOURCE(S): MARPAT 138:321578
GI



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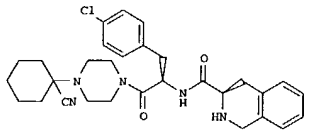
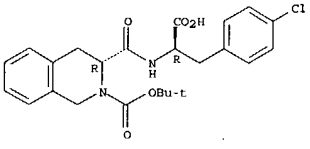


II

L4 ANSWER 39 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
AB The invention relates to peptides I [m = 1-4; n = 0-4; A is (un)substituted alkanediyl; R1, R2, R3a, R3b = H, (un)substituted alkyl, aryl, arylalkyl, heterocyclyl, or heterocyclylalkyl or may combine to form rings; R1 or R2 may also be acyl; R4 = (un)substituted (hetero)aryl; R5 = H, OH, (un)substituted alkyl, aryl, or heterocyclyl; R6 = cyano, nitro, (un)substituted heterocyclyl, amino, carbamoyl, etc.; R7 = H or 1-4 substituents], or stereoisomers, prodrugs or pharmaceutically-acceptable salts, which function as melanocortin receptor ligands and may be used to treat disorders or illnesses including cachexia, obesity, diabetes, inflammation, and sexual dysfunction. Thus, treatment of cyclohexanone with sodium metabisulfite in H2O, followed by addition of Boc-protected piperazine and then NaCN, afforded 1-Boc-4-(1-cyanocyclohexyl)piperazine. The latter was converted into peptide II via coupling reaction.
IT **252008-71-2**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of peptides as ligands of melanocortin receptors)
RN 252008-71-2 CAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3-[[[(1R)-1-carboxy-2-(4-chlorophenyl)ethyl]amino]carbonyl]-3,4-dihydro-, 2-(1,1-dimethylethyl) ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 40 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:300170 CAPLUS
DOCUMENT NUMBER: 139:143349
TITLE: Pharmacological Profiles of Peptide Drug Candidates for the Treatment of Alzheimer's Disease
AUTHOR(S): Adessi, Celine; Frossard, Marie-Jose; Boissard, Christophe; Fraga, Santiago; Bieler, Sylvain; Ruckle, Thomas; Vilbois, Francis; Robinson, Sandra M.; Mutter, Manfred; Banks, William A.; Soto, Claudio
CORPORATE SOURCE: Serono Pharmaceutical Research Institute, Geneva, 1228, Switz.
SOURCE: Journal of Biological Chemistry (2003), 278(16), 13905-13911
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

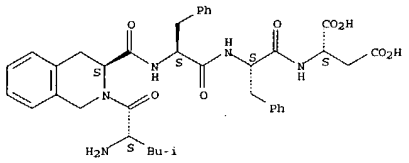
AB Amyloid plaques in brain, composed of aggregates of amyloid-β peptide, play a central role in the pathogenesis of Alzheimer's disease and represent a good target for treatment. We have shown previously that a 5-amino acid β-sheet breaker peptide (iAβ5p), end-protected, has the ability to induce a dramatic reduction in amyloid deposition in two different transgenic Alzheimer's models. The aim of this study was to evaluate the effect of chemical modifications of the peptide bonds at the metabolite cleavage sites on the pharmacol. properties of iAβ5p derivs. Using a rational approach, peptide analogs were designed and tested for in vitro activity and enzymic stability. One peptide analog containing a Me group introduced at the nitrogen atom of one amide bond showed increased stability in vitro, a 10-fold higher in vivo half-life, and good brain uptake compared with iAβ5p while maintaining a similar activity in vitro. Our results suggest that the pharmacol. profile of β-sheet breaker peptides can be improved to produce compds. with drug-like properties that might offer a new promise in the treatment of Alzheimer's disease.

IT **572914-18-2**
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. profiles of peptide drug candidates for treatment of Alzheimer's disease)

RN 572914-18-2 CAPLUS
CN L-Aspartic acid, L-leucyl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-phenylalanyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 40 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 41 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:178421 CAPLUS
DOCUMENT NUMBER: 138:349900
TITLE: Ochratoxin A Forms a Carbon-Bonded C8-Deoxyguanosine Nucleoside Adduct: Implications for C8 Reactivity by a Phenolic Radical
AUTHOR(S): Dai, Jian; Wright, Marcus W.; Manderville, Richard A.
CORPORATE SOURCE: Department of Chemistry, Wake Forest University, Winston-Salem, NC, 27109, USA
SOURCE: Journal of the American Chemical Society (2003), 125(13), 3716-3717
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

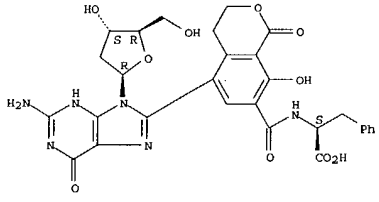
AB The ability of the carcinogenic fungal toxin Ochratoxin A (OTA) to react with deoxyguanosine (dG) has been assessed using electrospray mass spectrometry and NMR. Photoexcitation of OTA (100 μM) in the presence of 50 mol equiv of dG led to the isolation and identification of the C8-deoxyguanosine nucleoside adduct. Importantly, the same adduct was formed upon oxidative activation of OTA using horseradish peroxidase (HRP)/H2O2 or the transition metals Fe(II) and Cu(II), as evidenced by mass spectrometry. Because the mutagenicity and subsequent carcinogenicity of OTA are believed to stem from oxidative DNA damage (strand scission and oxidative base products) and formation of guanine-specific DNA adducts, the adduct confirms the ability of OTA to react covalently with dG and has important implications for the mechanism of action of OTA and other chlorophenolic toxins that undergo oxidation to yield phenoxyl radicals. The C8 position of dG is susceptible to radical attack, as was amply proven through formation of the hydroxyl radical-derived DNA lesion, 8-oxodeoxyguanosine. The adduct is the first structurally characterized nucleoside adduct of a chlorophenolic toxin, and its formation has important implications for the mutagenicity of phenolic xenobiotics.

IT **519005-04-0**
RL: BSU (Biological study, unclassified); FMU (Formation, unclassified); PRP (Properties); BIOL (Biological study); FORM (Formation, nonpreparative)
(ochratoxin A forms carbon-bonded C8-deoxyguanosine nucleoside adduct with implications for C8 reactivity by phenolic radical as mechanism for oxidative DNA damage)

RN 519005-04-0 CAPLUS
CN L-Phenylalanine, N-[[5-[2-amino-9-(2-deoxy-β-D-erythro-pentofuranosyl)-6,9-dihydro-6-oxo-1H-purin-8-yl]-3,4-dihydro-8-hydroxy-1-oxo-1H-2-benzopyran-7-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 41 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



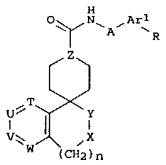
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 42 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:133239 CAPLUS
DOCUMENT NUMBER: 138:170086
TITLE: Preparation of spiro[isoquinoline-piperidine], spiro[indoline-piperidine], and spirocyclohexane compounds as antagonists of neuropeptide Y receptor
INVENTOR(S): Fukami, Takehiro; Nonoshita, Katsumasa; Sagara, Takeshi; Kishino, Hiroyuki
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 220 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003014083	A1	20030220	WO 2002-JP7922	20020802

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: JP 2001-239567 A 20010807
OTHER SOURCE(S): MARPAT 138:170086
GI



I

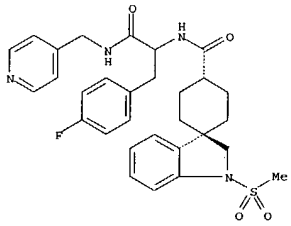
AB The invention relates to compds. such as spiro[cyclohexane-1,1'-(3'H)-isobenzofuran], spiro[4-, 5-, 6-, or 7-azaisobenzofuran-1(3H),1'-cyclohexane], spiro[indoline-3,1'-cyclohexane], spiro[indoline-3,4'-piperidine], spiro[isobenzofuran-1(3H),4'-piperidine], and spiro[isoquinoline-1(2H),4'-piperidine] represented by the general formula (I) or salts or esters thereof [A = linear C1-6 hydrocarbon group which

L4 ANSWER 42 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
may be substituted or interrupted by oxygen or nitrogen; Ar1 = (un)substituted aryl or heteroaryl; n = 0,1; R = H, lower alkylene; T, U, V, W = (un)substituted CH or N and at least 2 of T, U, V, and W is (un)substituted CH; X = -N(SO2R1)-, -N(COR2)-, or CO; Y = -C(R3)(R4)-, O, or -N(R5)-; and Z = CH or nitrogen; wherein R1 , R2, R5 = H, lower alkyl, aralkyl, aryl; R3, R4 = H, HO, lower alkyl, aralkyl, aryl]. These compds. exhibit neuropeptide Y (NPY) receptor antagonism and are therefore useful as treating agents for various diseases in which NPY participates such as circulatory diseases, central nervous system diseases, and metabolic diseases, in particular over eating (hyperphagia), obesity, and diabetes. Thus, 64 mg 4-phenylcyclohexylamine hydrochloride and 115 mg 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride were added to a soln. of 74 mg trans-3'-oxospiro[cyclohexane-1,1'(3'H)-isobenzofuran]-4-carboxylic acid in 2 mL pyridine and stirred at room temp. for 24 h to give trans-3'-oxo-N-(trans-4-phenylcyclohexyl)spiro[cyclohexane-1,1'(3'H)-isobenzofuran]-4-carboxamide (II). II and trans-N-[(S)-1-benzyl-2-(benzylamino)ethyl]-1-(methanesulfonyl)spiro[indoline-3,1'-cyclohexane]-4'-carboxamide showed IC50 of 2.5 and 0.69 nM for inhibiting the binding of [125I]peptide YY to human NPY Y5 receptor.

IT **497238-78-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of spiro[isoquinoline-piperidine], spiro[indoline-piperidine], and spiro[azaisobenzofuran-cyclohexane], and spirocyclohexane compds. as antagonists of neuropeptide Y receptor for treating overeating, obesity, and diabetes)

RN 497238-78-5 CAPLUS
CN Spiro[cyclohexane-1,3'-[3H]indole]-4-carboxamide, N-[1-[(4-fluorophenyl)methyl]-2-oxo-2-[(4-pyridinylmethyl)amino]ethyl]-1',2'-dihydro-1'-(methylsulfonyl)-, trans- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

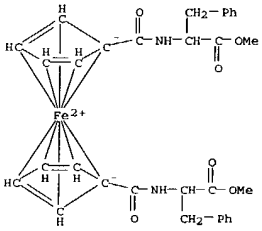
L4 ANSWER 43 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:126123 CAPLUS
DOCUMENT NUMBER: 139:69500
TITLE: Organometallic β-turn mimetics. A structural and spectroscopic study of inter-strand hydrogen bonding in ferrocene and cobaltocenium conjugates of amino acids and dipeptides
AUTHOR(S): van Staveren, Dave R.; Weyhermueller, Thomas; Metzler-Nolte, Nils
CORPORATE SOURCE: Max-Planck-Institut fuer Strahlenchemie, Muelheim/Ruhr, D-45470, Germany
SOURCE: Dalton Transactions (2003), (2), 210-220
CODEN: DTARAF; ISSN: 1477-9226
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 139:69500

AB By using organometallic turn-mimetics, the influence of a pos. charge on the structure and stability of peptide turn structures which are stabilized by H bonds. Starting from metallocene mono- (1) or dicarboxylic acid (2), 11 amide derivs. were prepared, CpM(C5H4-CO-Phe-OMe) (3), CpM(C5H4-CO-Ala-Phe-OMe) (4), CpM(C5H4-CO-NH-CHMe-Ph) (5), M(C5H4-CO-Phe-OMe)2 (6), M(C5H4-CO-Ala-Phe-OMe)2 (7), and Fe(C5H4-CO-NH-CHMe-Ph)2 (8a) with Cp = η-C5H5 and M = Fe (ferrocene, a) or M = Co+ (cobaltocenium, b). All compds. were characterized by elemental anal., MS, IR, electrochem., Mossbauer spectroscopy (a only) and NMR spectroscopy. Solid state structures of 4a, 6a, 7a, 3b, and 5b were determined by single crystal x-ray diffraction. 1H NMR data (δ(NH) and Δδ(NH) with T) as well as solution IR spectra were evaluated to determine intramol. H bond interactions in solution No intramol. H bonds form in the monosubstituted derivs. 3-5 and in 8a. For 7, a strong intramol. H bond is observed between the NHAla and COAla, of the other ring, forming an 11-membered ring in solution as well as in the solid state. The situation is most complex for 6, which forms an intramol. 8-membered ring by H bonds NHPhe···COCp in the solid state (6a), but a sym. 11-membered ring structure with NHPhe···COPhe' bonds in solution A comparison of the uncharged ferrocene derivs. with the iso-structural but pos. charged cobaltocenium deriv. reveals only minor differences. Apparently, the presence of a pos. charge does not significantly influence H bonds in peptide turn structures. The results are related to geometries and amino acid sequences in protein turn structures and a nomenclature for turn mimetics with a parallel orientation of the two peptide strands is proposed.

IT **181589-78-6P**
RL: CPS (Chemical process); PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(crystal structure, electrochem. redox, Mossbauer spectra; condensation reaction of ferrocene carboxylic acid derivs. with phenylethylamine, alanine ester and dipeptide in presence of coupling reagent to give amides)

RN 181589-78-6 CAPLUS
CN Ferrocene, 1,1'-bis[[[(1S)-2-methoxy-2-oxo-1-(phenylmethyl)ethyl]amino]carbonyl]- (9CI) (CA INDEX NAME)

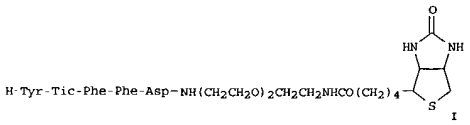
L4 ANSWER 43 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 44 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:89939 CAPLUS
DOCUMENT NUMBER: 138:271967
TITLE: A Solid-Phase Synthetic Strategy for Labeled Peptides: Synthesis of a Biotinylated Derivative of the δ Opioid Receptor Antagonist TIPP (Tyr-Tic-Phe-Phe-OH)
AUTHOR(S): Kumar, Vivek; Aldrich, Jane V.
CORPORATE SOURCE: Department of Pharmaceutical Sciences School of Pharmacy, University of Maryland, Baltimore, MD, 21201, USA
SOURCE: Organic Letters (2003), 5(5), 613-616
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:271967
GI



H-Tyr-Tic-Phe-Phe-Asp-NH(CH2CH2O)2CH2CH2NHCO(CH2)4-

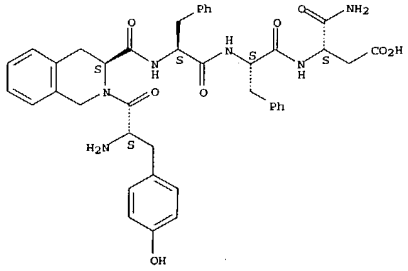
I

AB A general solid-phase synthetic strategy for labeled peptides was developed and used to prepare a biotinylated peptide I (Tic = 1,2,3,4-tetrahydroisoquinolinyl-3-carbonyl) analog of the δ opioid receptor antagonist TIPP (H-Tyr-Tic-Phe-Phe-OH). A monoprotected hydrophilic diamine linker was attached to an aldehyde-containing solid-phase resin by reductive amination, followed by introduction of biotin and peptide synthesis to yield biotinyl-peptide I. The high δ receptor affinity and selectivity of I demonstrate the applicability of this design approach for labeled peptide derivs.

IT **319906-09-7**
RL: BSU (Biological study, unclassified); BIOL (Biological study) (biol. activity comparisons at δ- and μ-opioid receptors)
RN 319906-09-7 CAPLUS
CN L-α-Asparagine, L-tyrosyl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-phenylalanyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 44 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 45 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:76750 CAPLUS
DOCUMENT NUMBER: 138:137595
TITLE: Preparation of N-[(aryl or thienyl)sulfonyl]dipeptide derivatives and analogs as α2β1 integrin inhibitors
INVENTOR(S): Takayanagi, Masaru; Fukuchi, Naoyuki; Sugiki, Masayuki; Futaki, Fumie; Takehana, Shunji; Kajigaya, Yuki; Takamatsu, Yayoi; Tokumasu, Munetaka; Yoshida, Kaoru
PATENT ASSIGNEE(S): Ajinomoto Co., Inc., Japan
SOURCE: PCT Int. Appl., 187 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003008380	A1	20030130	WO 2002-JP7250	20020717

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

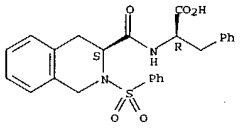
PRIORITY APPLN. INFO.: JP 2001-218507 A 20010718
JP 2001-351077 A 20011116
OTHER SOURCE(S): MARPAT 138:137595

AB The compds. represented by the following formula D-Y-N(L)-CH(B)-X-CH[(CH2)nA]COE [wherein n = an integer of 0-2; X = CH2O, CO2, each N-(un)substituted CH2NH, CONH, C(S)NH, or SO2NH, CH2S, CH2SO2; Y = CH2, CO, C(S), SO2, each N-(un)substituted NHCO or NHC(S); A, D = (un)substituted Ph, aryl, heteroaryl; B = (un)substituted amino-lower alkyl or carbamoyl-lower alkyl; L = H, lower alkyl, lower alkenyl, lower alkynyl, cycloalkyl or cycloalkyl-lower alkyl optionally containing a heteroatom in the ring, aryl, heteroaryl, aryl-lower alkyl, heteroaryl-lower alkyl, halo-lower alkyl, hydroxy-lower alkyl, lower alkoxy-lower alkyl, mercapto-lower alkyl, lower alkylthio-lower alkyl, (un)substituted amino-lower alkyl, carboxy-lower alkyl, lower alkoxycarbonyl-lower alkyl, (un)substituted carbamoyl-lower alkyl; E = HO, lower alkoxy, (un)substituted amino, hydroxylaminol or pharmacol. acceptable salts thereof are prepared These compds. have α2β1 integrin inhibitory activity (inhibition of binding between platelet GPIa/IIa receptor and collagen) and are useful as antiplatelet agents for the prevention or treatment of various diseases such as myocardial infarction, angina pectoris, acute coronary syndrome, peripheral artery obstruction, deep venous thrombosis, cerebral infarction, stroke, and pulmonary embolism. Thus, N-(4-nitrobenzenesulfonyl)-L-prolyl-L-4-aminophenylalanine (prepared by the Fmoc solid phase method) showed IC50 of 2.0 μg/mL for inhibiting the binding of collagen to platelet GPIa/IIa receptor.

IT **493040-65-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (prepn. of N-[(aryl or thienyl)sulfonyl]dipeptide derivs. and analogs as α2β1 integrin inhibitors and antiplatelet agents for the prevention or treatment of various diseases)
RN 493040-65-6 CAPLUS
CN D-Phenylalanine, N-[[(3S)-1,2,3,4-tetrahydro-2-(phenylsulfonyl)-3-isoquinolinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 45 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

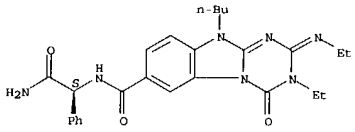
L4 ANSWER 46 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:24837 CAPLUS
DOCUMENT NUMBER: 138:221561
TITLE: Parallel Solid-Phase Synthesis of 2-Imino-4-oxo-1,3,5-triazino[1,2-a]benzimidazoles via Tandem Aza-Wittig/Heterocumulene-Mediated Annulation Reaction
AUTHOR(S): Hoesl, Cornelia E.; Nefzi, Adel; Houghten, Richard A.
CORPORATE SOURCE: Torrey Pines Institute for Molecular Studies, San Diego, CA, 92121, USA
SOURCE: Journal of Combinatorial Chemistry (2003), 5(2), 155-160
CODEN: JCCHFF; ISSN: 1520-4766
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:221561

AB The parallel synthesis of a large number of 2-imino-4-oxo-1,3,5-triazino[1,2-a]benzimidazole derivs. via a solid-phase 1,3,5-triazine annulation reaction is described. The solid-phase approach involves the in situ generation of iminophosphorane derivs. derived from resin-bound 2-aminobenzimidazoles employing Mitsunobu conditions. The subsequent Aza-Wittig reaction of the iminophosphoranes with isocyanates leads to highly reactive carbodiimides, which undergo an intramol. heterocyclization reaction to form tetrasubstituted 2-imino-4-oxo-1,3,5-triazino[1,2-a]benzimidazoles in high yields (74-94%) and good purity (>80%).

IT **500732-13-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(parallel solid-phase synthesis of 2-imino-4-oxo-1,3,5-triazino[1,2-a]benzimidazoles via tandem aza-Wittig/heterocumulene-mediated annulation reaction)

RN 500732-13-8 CAPLUS
CN 1,3,5-Triazino[1,2-a]benzimidazole-7-carboxamide, N-[(1S)-2-amino-2-oxo-1-phenylethyl]-10-butyl-3-ethyl-2-(ethylimino)-2,3,4,10-tetrahydro-4-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

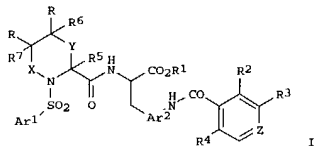


REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 47 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:23531 CAPLUS
DOCUMENT NUMBER: 138:90079
TITLE: Preparation of N-arylsulfonyl aza-bicyclic derivatives as potent cell adhesion inhibitors
INVENTOR(S): Lin, Linus S.; Doherty, George; Shah, Shrenik K.; Chang, Linda L.; Hagmann, William K.; Mumford, Richard A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 31 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003008861	A1	20030109	US 2002-96607	20020313
PRIORITY APPLN. INFO.:			US 2001-277233P P	20010320

OTHER SOURCE(S): MARPAT 138:90079
GI



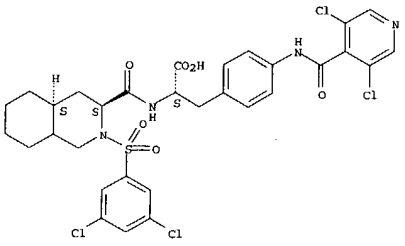
I

AB Compds. I [R2 is an (un)substituted cycloalkyl or heterocyclyl ring; R1 = H, alkyl, arylalkyl; R2, R4 = halo, alkyl, alkoxy; R3 = H, OH, MeO, NH2; Z = N or N:O; Ar1 = (un)substituted Ph, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, or triazinyl; Ar2 = 1,4-phenylene or 2,5-pyridylene; X, Y = (CH2)0-2; R5 = H, alkyl; R6, R7 = H, alkyl, OH, alkoxy, carboxy, amino, sulfonylamino, etc.] or their pharmaceutically-acceptable salts were prepared as antagonists of VLA-4 and/or α4/β7 and as such are useful in the inhibition or prevention of cell adhesion and cell-adhesion mediated pathologies. Thus, N-[N-(3,5-dichlorobenzenesulfonyl)octahydroisoindole-1-carbonyl]-4-[(3,5-dichloroisonicotinoyl)amino]-L-phenylalanine was prepared by coupling of N-(3,5-dichlorobenzenesulfonyl)octahydroisoindole-1-carboxylic acid chloride with 4-[(3,5-dichloroisonicotinoyl)amino]-L-phenylalanine tert-Bu ester (syntheses given), followed by separation of diastereomers and ester cleavage.

IT **483364-66-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-arylsulfonyl heteroaroyl amino acid derivs. as cell adhesion inhibitors)

L4 ANSWER 47 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 483364-66-5 CAPLUS
CN L-Phenylalanine, N-[[(3S,4aS)-2-[(3,5-dichlorophenyl)sulfonyl]decahydro-3-isoquinolinyl]carbonyl]-4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



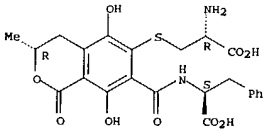
L4 ANSWER 48 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2003:11879 CAPLUS
DOCUMENT NUMBER: 139:97307
TITLE: Photochemically catalyzed reaction of ochratoxin A with D- and L-cysteine
AUTHOR(S): Brow, Mark E.; Dai, Jian; Park, Gyungse; Wright, Marcus W.; Gillman, Ivan G.; Manderville, Richard A.
CORPORATE SOURCE: Department of Chemistry, Wake Forest University, Winston-Salem, NC, 27109-7486, USA
SOURCE: Photochemistry and Photobiology (2002), 76(6), 649-656
CODEN: PHCBAP; ISSN: 0031-8655
PUBLISHER: American Society for Photobiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The photolysis (>300 nm) of ochratoxin A (OTA, N-{[(3R)-5-chloro-8-hydroxy-3-methyl-1-oxo-7-isochromanyl]carbonyl}- 3-phenyl-L-alanine, 1) in the presence of excess (2 and 12 molar equiv) cysteine (CySH) has been investigated and found to yield sulfur adducts 5 and 6 that are characterized by liquid chromatog.-mass spectrometry and 1H-NMR spectroscopy. The adduct 5 was ascribed to the Michael addition conjugate resulting from covalent attachment of CySH to the ochratoxin quinone (4) generated by photooxidn. of OTA. This species was also formed by photolysis of a synthetic sample of the hydroquinone of OTA (ochratoxin hydroquinone, 3) in the presence of 12 equiv L-CySH. The conjugate 5 derived from photolysis of 3 with L-CySH was used for 1H-NMR anal. The sulfur adduct 6 was the major species detected from covalent attachment of CySH to photoactivated OTA, and it resulted from direct displacement of the OTA Cl atom by CySH. The implications of the cysteinyl adducts to the in vivo toxicity of OTA are discussed, with particular emphasis given to conjugate 5, as products from the photooxidative pathway may be of relevance to the nephrotoxic properties of OTA.

IT **560134-09-0P**
RL: FMU (Formation, unclassified); PRP (Properties); PUR (Purification or recovery); FORM (Formation, nonpreparative); PREP (Preparation)
(photochem. catalyzed reaction of ochratoxin A with D- and L-cysteine)

RN 560134-09-0 CAPLUS
CN L-Phenylalanine, N-[[(3R)-6-[[(2R)-2-amino-2-carboxyethyl]thio]-3,4-dihydro-5,8-dihydroxy-3-methyl-1-oxo-1H-2-benzopyran-7-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 49 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

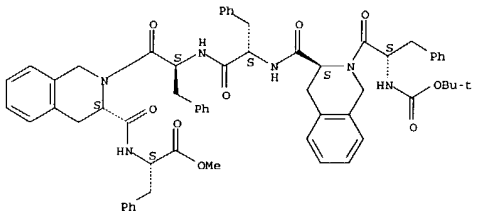
ACCESSION NUMBER: 2003:146 CAPLUS
DOCUMENT NUMBER: 138:205334
TITLE: Novel Antibiotics: Macrocyclic Peptides Designed to Trap Holliday Junctions
AUTHOR(S): Bolla, Megan L.; Azevedo, Enrique V.; Smith, Jason M.; Taylor, Rachel E.; Ranjit, Dev K.; Segall, Anca M.; McAlpine, Shelli R.
CORPORATE SOURCE: Department of Chemistry, Molecular Biology Institute and Center for Applied and Experimental Genomics, San Diego State University, San Diego, CA, 92182-1030, USA
SOURCE: Organic Letters (2003), 5(2), 109-112
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:205334

AB This work describes the synthesis of eight macrocyclic peptides designed to trap Holliday junctions in bacteria, thereby inhibiting bacterial growth. These macrocycles were designed from linear dimerized hexapeptides that bind to the C-2 sym. Holliday junction. They were synthesized from three monomers using a combinatorial-like strategy that permits elucidation of the monomer role in accumulation of Holliday junctions and antibiotic activity. These macrocycles are an important step in designing and synthesizing a new class of antibiotics.

IT **617688-75-2P**
RL: CPN (Combinatorial preparation); CRT (Combinatorial reactant); RCT (Reactant); SPN (Synthetic preparation); CMBI (Combinatorial study); PREP (Preparation); RACT (Reactant or reagent)
(combinatorial-style preparation and activity of macrocyclic antibacterial peptides designed to trap Holliday junctions in bacteria)

RN 617688-75-2 CAPLUS
CN L-Phenylalanine, N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-phenylalanyl-L-phenylalanyl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



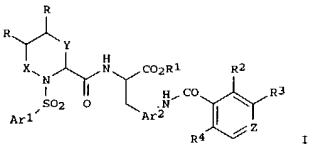
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS

L4 ANSWER 50 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:965131 CAPLUS
DOCUMENT NUMBER: 138:24961
TITLE: Preparation of N-arylsulfonyl aryl aza-bicyclic derivatives as potent cell adhesion inhibitors
INVENTOR(S): Lin, Linus S.; Shah, Shrenik K.; Chang, Linda L.; Hagmann, William K.; Mumford, Richard A.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 19 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002193399	A1	20021219	US 2002-97028	20020313
US 6559174	B2	20030506		

PRIORITY APPLN. INFO.: US 2001-277235P P 20010320
OTHER SOURCE(S): MARPAT 138:24961
GI



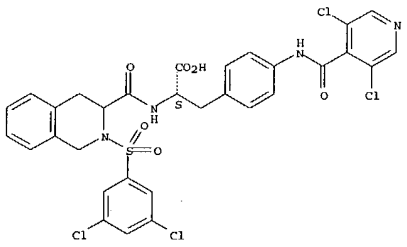
I

AB Compds. I [R2 is an (un)substituted (hetero)aryl ring; R1 = H, alkyl, arylalkyl; R2, R4 = halo, alkyl, alkoxy; R3 = H, OH, MeO, NH2; Z = N or N:O; Ar1 = (un)substituted Ph, pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, or triazinyl; Ar2 = 1,4-phenylene or 2,5-pyridylene; X, Y = (CH2)0-2] or their pharmaceutically-acceptable salts were prepared as antagonists of VLA-4 and/or α4/β7 and as such are useful in the inhibition or prevention of cell adhesion and cell-adhesion mediated pathologies. Thus, N-[N-(4-methylbenzenesulfonyl)-1,3-dihydro-2H-isoindole-1-carbonyl]-4-[(3',5'-dichloroisonicotinoyl)amino]-L-phenylalanine was prepared by coupling of N-(4-methylbenzenesulfonyl)-1,3-dihydro-2H-isoindole-1-carboxylic acid with 4-[(3',5'-dichloroisonicotinoyl)amino]-L-phenylalanine tert-Bu ester (syntheses given), followed by ester cleavage using TFA.

IT **478170-92-2P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-arylsulfonyl heteroaroyl amino acid derivs. as cell adhesion inhibitors)

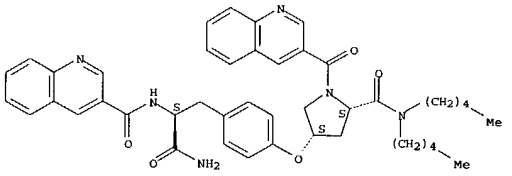
RN 478170-92-2 CAPLUS
CN L-Phenylalanine, N-[[2-[(3,5-dichlorophenyl)sulfonyl]-1,2,3,4-tetrahydro-3-isoquinolinyl]carbonyl]-4-[[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 51 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:943602 CAPLUS
DOCUMENT NUMBER: 138:385709
TITLE: Identification of TNF-α inhibitors from a split-pool library based on a tyrosine-proline peptidomimetic scaffold
AUTHOR(S): Jackson, Randy W.; Tabone, John C.; Howbert, J. Jeffry
CORPORATE SOURCE: Department of Chemistry, Celltech R&D, Inc., Bothell, WA, 98021, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(2), 205-208
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:385709
AB The design and synthesis of a combinatorial library based on a 4-aryloxyproline scaffold with tyrosine as the aryl portion is described. The 1728 member library was prepared using the split-pool method to generate pools of compds. Screening of the library components as mixts. followed by deconvolution led to the discovery of novel inhibitors of TNF-α induced apoptosis.
IT **526223-58-5P**
RL: BSU (Biological study, unclassified); CPN (Combinatorial preparation); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation)
(preparation of peptide library based on tyrosine-proline peptidomimetic scaffold and identification of TNF inhibitors)
RN 526223-58-5 CAPLUS
CN 3-Quinolinecarboxamide, N-[(1S)-2-amino-1-[[4-[[(3S,5S)-5-[(dipentylamino)carbonyl]-1-(3-quinolinylcarbonyl)-3-pyrrolidinyl]oxy]phenyl]methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 52 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:928230 CAPLUS
DOCUMENT NUMBER: 138:19472
TITLE: Method of identifying inhibitors of Cdc25 using three dimensional crystal structure of the catalytic domain of Cdc25
INVENTOR(S): Taylor, Neil R.; Borhani, David; Epstein, David; Rudolph, Johannes; Ritter, Kurt; Fujimori, Taro; Robinson, Simon; Eckstein, Jens; Haupt, Andreas; Walker, Nigel; Dixon, Richard W.; Choquette, Deborah; Blanchard, Jill; Kluge, Arthur; Pal, Kollol; Bockovich, Nicholas; Come, Jon; Hediger, Mark
PATENT ASSIGNEE(S): Australia
SOURCE: U.S. Pat. Appl. Publ., 246 pp., Cont.-in-part of U.S. Ser. No. 645,750.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

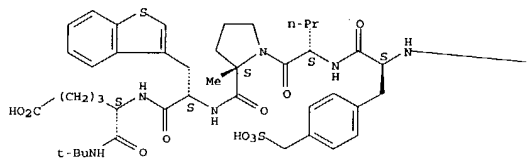
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002183249	A1	20021205	US 2001-797500	20010301
PRIORITY APPLN. INFO.:			US 1999-172215P P	19990831
			US 2000-645750 A2	20000824

OTHER SOURCE(S): MARPAT 138:19472
AB The present invention relates to the x-ray crystallog. study of proteins comprising the catalytic domains of Cdc25. The atomic coordinates which result from this study are of use in identifying compds. which fit in the catalytic domain and are, therefore, potential inhibitors of Cdc25. The present invention further provides proteins which comprise the ligand binding domain of Cdc25, crystalline forms of these proteins and the use of these crystalline forms to determine the three dimensional structure of the catalytic domain of Cdc25. The invention also relates to the use of the three dimensional structure of the Cdc25 catalytic domain in methods of designing and/or identifying potential inhibitors of Cdc25 activity, for example, compds. which inhibit the binding of a native substrate to the Cdc25 catalytic domain. These Cdc25 inhibitors are of use in methods of treating a patient having a condition which is modulated by Cdc25 activity, for example, a condition characterized by excessive, inappropriate or undesirable cellular proliferation such as cancer.
IT **477908-84-2P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(method of identifying inhibitors of Cdc25 using three dimensional crystal structure of catalytic domain of Cdc25)
RN 477908-84-2 CAPLUS
CN L-Norvalinamide, N-(4-dibenzofuranylcarbonyl)-4-(sulfomethyl)-L-phenylalanyl-L-norvalyl-2-methyl-L-prolyl-3-benzo[b]thien-3-yl-L-alanyl-5-carboxy-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

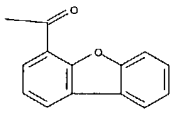
Absolute stereochemistry.

L4 ANSWER 52 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



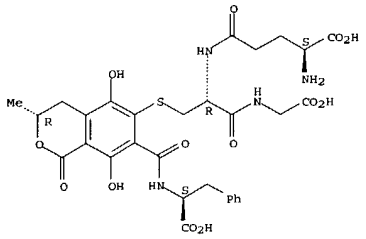
PAGE 1-B



L4 ANSWER 53 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:850472 CAPLUS
DOCUMENT NUMBER: 138:68223
TITLE: Detection and Characterization of a Glutathione Conjugate of Ochratoxin A
AUTHOR(S): Dai, Jian; Park, Gyungse; Wright, Marcus W.; Adams, Marissa; Akman, Steven A.; Manderville, Richard A.
CORPORATE SOURCE: Department of Chemistry, Wake Forest University, Winston-Salem, NC, 27109-7486, USA
SOURCE: Chemical Research in Toxicology (2002), 15(12), 1581-1588
CODEN: CRTOEC; ISSN: 0893-228X
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ability of the carcinogenic mycotoxin ochratoxin A (OTA) to react with reduced glutathione (GSH) has been assessed using electrospray ionization (ES)-MS techniques. On the basis of the assumption that OTA undergoes biotransformation into the reactive quinone species, ochratoxin quinone (OTQ), a synthetic sample of the reduced form of OTQ, ochratoxin hydroquinone (OTHQ), was prepared and photoreacted with 6 M equiv of GSH to yield an authentic sample of the conjugate that was definitively identified by mass spectrometry, UV-vis spectroscopy and NMR. With the authentic sample of the conjugate in hand, it was demonstrated that the same conjugate is produced from reaction of 100 μM OTA (1) in the presence of 5 mM GSH following incubation for 1 h with either horseradish peroxidase (HRP)/H2O2, rat liver microsomes (RLM)/NADPH or free Fe(II). In each of these oxidative systems the conjugate was generated in less than 1% yield and the parent OTA mol. is poorly metabolized. Comparison of the peak area ratio of the conjugate to that for the hydroxyOTA metabolite from the RLM/NADPH system implied that the conjugate was produced at a rate of .apprx.1-3 pmol min-1 (mg of protein)-1. These studies are the first to demonstrate that OTA undergoes biotransformation to a reactive intermediate [OTQ] that covalently reacts with GSH to yield the conjugate. The biol. implications of the reactivity of OTA toward GSH are discussed.
IT **481053-26-3**
RL: ANT (Analyte); BSU (Biological study, unclassified); FMU (Formation, unclassified); PRP (Properties); ANST (Analytical study); BIOL (Biological study); FORM (Formation, nonpreparative)
(detection, characterization and biol. implications of glutathione conjugate of ochratoxin A as biotransformation product)
RN 481053-26-3 CAPLUS
CN Glycine, L-γ-glutamyl-S-[(3R)-7-[[[(1S)-1-carboxy-2-phenylethyl]amino]carbonyl]-3,4-dihydro-5,8-dihydroxy-3-methyl-1-oxo-1H-2-benzopyran-6-yl]-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 53 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 54 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

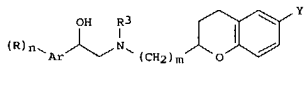
ACCESSION NUMBER: 2002:832787 CAPLUS
DOCUMENT NUMBER: 137:337786
TITLE: Preparation of chiral alkylaminochroman derivatives as β3-adrenoreceptor agonists
INVENTOR(S): O'Connor, Stephen J.; Ladouceur, Gaetan H.; Bullock, William H.; Campbell, Ann-Marie; Dai, Miao; Dally, Robert; Dumas, Jacques; Hatoum-Mokdad, Holia N.; Khire, Uday; Lee, Wendy; Liu, Qingjie; Lowe, Derek B.; Magnuson, Steven R.; Qi, Ning; Shelekhin, Tatiana E.; Shen, Quanrong; Smith, Roger A.; Wang, Ming
PATENT ASSIGNEE(S): Bayer Corporation, USA
SOURCE: PCT Int. Appl., 193 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002085891	A1	20021031	WO 2002-US12940	20020422
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003078260	A1	20030424	US 2002-131448	20020422
US 6660752	B2	20031209		
EP 1389202	A1	20040218	EP 2002-723958	20020422
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004072828	A1	20040415	US 2003-666903	20030917

PRIORITY APPLN. INFO.: US 2001-285719P P 20010423
US 2001-324518P P 20010926
US 2002-131448 A1 20020422
WO 2002-US12940 W 20020422

OTHER SOURCE(S): MARPAT 137:337786
GI

L4 ANSWER 54 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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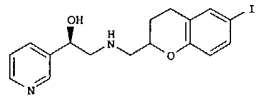


II

AB This invention relates to novel 2,6-substituted chroman derivs. which are useful in the treatment of β3-adrenoreceptor mediated conditions. Title compds. I [wherein R = independently OH, :O, halo, CN, NO2, (halo)alkyl, CF3, NR1R1, SR1, OR1, SO2R2, OCOR2, NR1COR2, COR2, NR1SO2R2, or (un)substituted Ph or heterocyclyl; R1 = independently H, (CH2)mO(CH2)mR5, or (un)substituted (cyclo)alkyl, Ph, or naphthyl; or NR1R1 = heterocyclyl; R2 = independently R1, OR1, NR1R1, or (un)substituted NHSO0-2-Ph, NHSO0-2-naphthyl, NHSO0-2-alkyl, or heterocyclyl; R3 = H, alkyl, or COR3; R4 = H, alkyl(phenyl), or alkylpyridyl; R5 = H or CO2H; R6 = H or (un)substituted alkyl or alkyl-SO0-2-alkyl; Ar = Ph or (fused) hetero(aryl); Y = halo, NO2, R6, SR1, SO0-2C6H4CO2R1, (CONR4CR4R4)pCO2R1, or (un)substituted Ph or heterocyclyl; m = 1-3; n = 0-5; p = 1 or 2; and pharmaceutically acceptable salts and esters thereof] were prepared as β3-adrenoceptor agonists. For example, coupling of (2R)-6-iodo-3,4-dihydro-2H-chromene-2-carboxylic acid and (1R)-2-amino-1-(3-pyridinyl)ethanol•2HCl with 1-hydroxybenzotriazole, 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide•HCl, and TEA in CH2Cl2 gave the amide (74%). Reduction using borane-dimethylsulfide complex in THF afforded the chromanmethaneamine II (84%). Over one hundred compds. of the invention demonstrated β3-adrenergic receptor agonist activity with EC50 values ≤ 1μM. I are useful in the treatment of β3-adrenergic receptor mediated conditions, including obesity, diabetes, gastrointestinal disorders, cardiovascular disorders, and urinary disorders (no data).

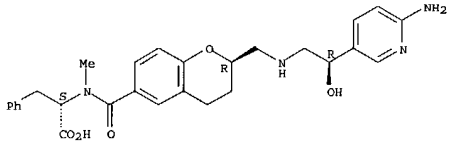
IT **474114-60-8P**, N-[[(2R)-2-[[[(2R)-2-(6-Amino-3-pyridinyl)-2-hydroxyethyl]amino]methyl]-3,4-dihydro-2H-chromen-6-yl]carbonyl]-N-methyl-L-phenylalanine
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(β3-adrenoreceptor agonist; preparation of chiral alkylaminochroman derivs. as β3-adrenoreceptor agonists)

RN 474114-60-8 CAPLUS

CN L-Phenylalanine, N-[[(2R)-2-[[[(2R)-2-(6-amino-3-pyridinyl)-2-hydroxyethyl]amino]methyl]-3,4-dihydro-2H-1-benzopyran-6-yl]carbonyl]-N-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 54 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

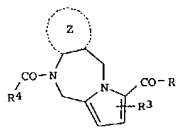
L4 ANSWER 55 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:814137 CAPLUS
DOCUMENT NUMBER: 137:325439
TITLE: Preparation of hydroxy cyclohexenylphenyl benzopyrrolodiazepine and triazabenzoazulene carboxamides as tocolytic oxytocin receptor antagonists
INVENTOR(S): Failli, Amedeo Arturo; Sanders, William Jennings; Trybulski, Eugene John
PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., USA
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002083679	A1	20021024	WO 2002-US11529	20020411
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002183311	A1	20021205	US 2002-119973	20020410
EP 1385849	A1	20040204	EP 2002-721727	20020411
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2001-283316P P 20010412
WO 2002-US11529 W 20020411
OTHER SOURCE(S): MARPAT 137:325439
GI

L4 ANSWER 55 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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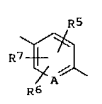
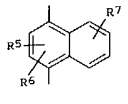


II



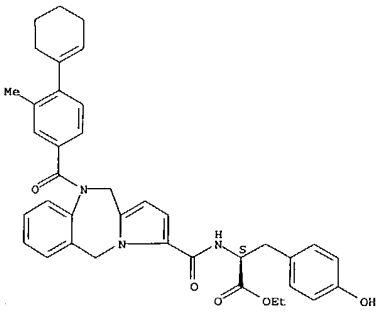
III

AB The present invention provides substituted 10,11-Dihydro-5H-benzo[e]pyrrolo[1,2-a][1,4]diazepine and 9,10-Dihydro-4H-3a,5,9-triazabenzo[f]azulene compds. (shown as I; 10-(5-chloro-4-(cyclohex-1-enyl)-2-methoxybenzoyl)-N-methyl-N-((2S,3R,4R,5R)-2,3,4,5,6-pentamethoxyhexyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carboxamide) as well as methods and pharmaceutical compns. using these compds. for the treatment and/or prevention and/or suppression of disorders which may be remedied or alleviated by oxytocin antagonist activity, including prevention and/or suppression of preterm labor, suppression of labor at term prior to cesarean deliver, and for the treatment of dysmenorrhea. These compds. are also useful in enhancing fertility rates, enhancing survival rates and synchronizing estrus in farm animals. In I: the Z ring is R1- and R2-substituted o-phenylene or 2,3-pyridinediyl; R1 and R2 are H, (C1-C6)alkyl, halo, cyano, trifluoromethyl, hydroxy, amino, (C1-C6)alkylamino, (C1-C6)alkoxy, -OCF3, (C1-C6alkoxy)carbonyl, -NHCO[(C1-C6)alkyl], carboxy, -CONH2, -CONH(C1-C6)alkyl, or -CON[(C1-C6)alkyl]2. R3 is H, (C1-C6)alkyl, (C1-C6)alkoxy, hydroxy, amino, (C1-C6)alkylamino, -COalkyl(C1-C6), or halo. R4 is B-C wherein B is II and III and C is (un)substituted cyclohexenyl, 3,4-dihydro-1-naphthyl or 5,6-dihydro-8-quinolinyl where A is CH or N; R5, R6, and R7 are H, (C1-C6)alkyl, (C1-C6)-alkoxy, hydroxy(C1-C6)alkyl, loweralkoxy(C1-C6)alkyl, (C2-C7)acyloxy(C1-C6)alkyl, (C1-C6alkyl)carbonyl, (C2-C6)alkenyl, (C2-C6)alkynyl, (C3-C8)cycloalkyl, formyl, (C3-C8)cycloalkylcarbonyl, carboxy, loweralkoxycarbonyl, (C3-C8)cycloalkyloxycarbonyl, (arylloweralkyl)oxycarbonyl, carbamoyl, -OCH2CH:CH2, halogen, haloloweralkyl including trifluoromethyl, -OCF3, -S(lower alkyl), -OC(O)N(lower alkyl)2, -CONH(lower alkyl), -CON(lower alkyl)2, lower alkylamino, diloweralkylamino, diloweralkylaminoloweralkyl, hydroxy, cyano, trifluoromethylthio, nitro, amino, lower alkylsulfonyl, aminosulfonyl, lower alkylaminosulfonyl, (un)substituted 2-dioxolanyl, Ph or naphthyl. R is acyclic or cyclic amino as defined in the claims. Although the methods of preparation are not claimed, 17 example prepns. are included. Binding to membranes of Chinese Hamster Ovary (CHO) cell line stably transfected with human vasopressin V1a receptor subtype, human vasopressin V2 receptor subtype and human oxytocin receptor by .apprx.17 I are reported.

IT **473665-66-6P**, (2S)-2-[[10-(4-(Cyclohex-1-enyl)-3-methylbenzoyl)-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepine-3-carbonyl]amino]-3-(4-hydroxyphenyl)propionic acid ethyl ester
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(drug candidate; preparation of hydroxy cyclohexenylphenyl benzopyrrolodiazepine and triazabenzoazulene carboxamides as tocolytic oxytocin receptor antagonists)

RN 473665-66-6 CAPLUS
CN L-Tyrosine, N-[[10-[4-(1-cyclohexen-1-yl)-3-methylbenzoyl]-10,11-dihydro-5H-pyrrolo[2,1-c][1,4]benzodiazepin-3-yl]carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 56 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:696111 CAPLUS
DOCUMENT NUMBER: 137:228607
TITLE: Crystal structure and three-dimensional structure of human Cdc25 catalytic domains and its use in designing peptidomimetic inhibitors
INVENTOR(S): Taylor, Neil R.; Borhani, David; Epstein, David; Rudolph, Johannes; Ritter, Kurt; Fujimori, Taro; Robinson, Simon; Eckstein, Jens; Haupt, Andreas; Walker, Nigel; Dixon, Richard W.; Choquette, Deborah; Blanchard, Jill; Kluge, Arthur; Pal, Kollol; Bockovich, Nicholas; Come, Jon; Hediger, Mark
PATENT ASSIGNEE(S): BASF Aktiengesellschaft, Germany; GPC Biotech Inc.
SOURCE: PCT Int. Appl., 351 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002070680	A1	20020912	WO 2001-US6587	20010301
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: WO 2001-US6587 20010301
OTHER SOURCE(S): MARPAT 137:228607

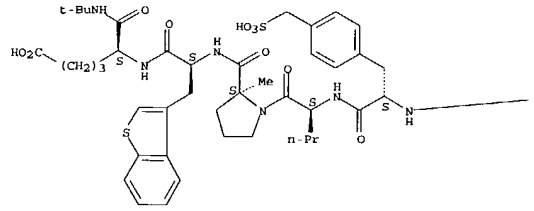
AB Due to its role in regulating the cell cycle, Cdc25 (a family of dual specificity phosphatases) is a potential target for therapies aimed at controlling proliferative diseases, but rational, structure-based design has not been possible because of the lack of accurate 3-dimensional data. The present invention relates to polypeptides which comprises the ligand binding domain of human Cdc25 proteins, crystalline forms of these polypeptides, and the use of these crystalline forms to determine the 3-dimensional structure of the catalytic domain of Cdc25. In particular, a high resolution crystal structure was obtained for the polypeptide denoted CDC25B(AN8B), comprising residues Glu-368 through Arg-562 of human Cdc25B, complexed with a pentapeptide inhibitor denoted cdc1249 (2-methoxynaphthyl-1-carboxy-(4-sulfomethyl)-L-Phe-L-Glu-L-Glu-L-naphthylalanine-L-Glu-amide). The invention also relates to the use of the 3-dimensional structure of the Cdc25 catalytic domain in methods of designing and/or identifying potential inhibitors of Cdc25 activity, for example, compds. which inhibitors of Cdc25 activity, for example, compds. which inhibit the binding of a native substrate to the Cdc25 catalytic domain. The syntheses and structures of a large number of putative pentapeptide inhibitors are also provided. Such inhibitors have potential in the treatment of diseases associated with excessive cellular proliferation, such as cancer, restenosis, reocclusion of coronary artery, and inflammation.

IT **329274-06-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(crystal structure and three-dimensional structure of human Cdc25 catalytic domains and its use in designing peptidomimetic inhibitors)

L4 ANSWER 56 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 329274-06-8 CAPLUS
CN L-Norvalinamide, N-(1-dibenzofuranylcarbonyl)-4-(sulfomethyl)-L-phenylalanyl-L-norvalyl-2-methyl-L-prolyl-3-benzo[b]thien-3-yl-L-alanyl-5-carboxy-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



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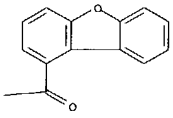
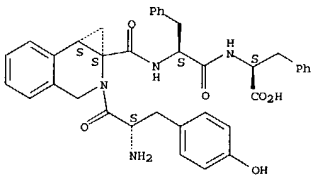


REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 57 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:692540 CAPLUS
DOCUMENT NUMBER: 138:338460
TITLE: Modifications of the Tic residue in TIPP-peptides
AUTHOR(S): Tourwe, D.; Van Cauwenberghe, S.; Vanommeslaeghe, K.; Mannekens, E.; Geerlings, P.; Toth, G.; Peter, A.; Csombos, J.
CORPORATE SOURCE: Department of Organic Chemistry, Vrije Universiteit Brussel, Brussels, B-1050, Belg.
SOURCE: Peptides: The Wave of the Future, Proceedings of the Second International and the Seventeenth American Peptide Symposium, San Diego, CA, United States, June 9-14, 2001 (2001), 683-684. Editor(s): Lebl, Michal; Houghten, Richard A. American Peptide Society: San Diego, Calif.
CODEN: 69DBAL, ISBN: 0-9715560-0-8
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A symposium report. Four 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid (Tic) analogs were prepared and used as replacements for Tic in the selective δ-opioid antagonist H-Tyr-Tic-Phe-Phe-OH (TIPP). Mol. modeling of tripeptide TIP analogs containing modified Tics with (3S) configuration indicated that the exact distance between the aromatic rings in TIP and the positioning of the phenolic group are crucial for δ-affinity. The positioning of the Tic carbonyl also determined the orientation of the Phe residue.
IT **517891-95-1P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(modifications of Tic residue in TIPP-peptides)
RN 517891-95-1 CAPLUS
CN L-Phenylalanine, L-tyrosyl-(1aS,7bS)-1,2,3,7b-tetrahydro-1aH-cycloprop[c]isoquinoline-1a-carbonyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

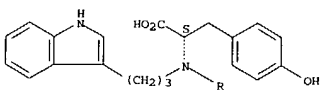
Absolute stereochemistry.

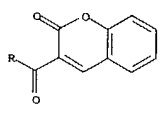


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 58 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:692518 CAPLUS
DOCUMENT NUMBER: 138:268230
TITLE: Design, synthesis and biological evaluation of pilicides: inhibitors of pilus assembly in pathogenic bacteria
AUTHOR(S): Larsson, Andreas; Emtenaes, Hans; Svensson, Anette; Pinkner, Jerome S.; Hultgren, Scott J.; Almqvist, Fredrik; Kihlberg, Jan
CORPORATE SOURCE: Department of Organic Chemistry, Umea University, Umea, SE-901 87, Swed.
SOURCE: Peptides: The Wave of the Future, Proceedings of the Second International and the Seventeenth American Peptide Symposium, San Diego, CA, United States, June 9-14, 2001 (2001), 636-637. Editor(s): Lebl, Michal; Houghten, Richard A. American Peptide Society: San Diego, Calif.
CODEN: 69DBAL, ISBN: 0-9715560-0-8
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A crystal structure of the complex between the periplasmic chaperone PapD, involved in assembly of P Pili in uropathogenic Escherichia coli, and a 19-mer peptide corresponding to the C-terminus of the adhesin PapG was used to develop two classes of peptidomimetics as potential inhibitors of the chaperone/subunit complex by rational drug design. The amino acid derivs. were synthesized through an N-alkylation of an amino acid followed by acylation of the resulting secondary amine. The 2-pyridinones were obtained via a novel procedure based on the use of acid chlorides and nitriles as starting materials. Within the amino acid derivs. and 2-pyridinones, which bind to periplasmic chaperones and even dissociate chaperone, pilus subunit complexes were detected.
IT **503305-58-6**
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(design and synthesis and biol. evaluation of pilicides such as inhibitors of pilus assembly in pathogenic bacteria that dissociate periplasmic chaperone-pilus subunit complexes)
RN 503305-58-6 CAPLUS
CN L-Tyrosine, N-[3-(1H-indol-3-yl)propyl]-N-[(2-oxo-2H-1-benzopyran-3-yl)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.





L4 ANSWER 58 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 59 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:637480 CAPLUS
DOCUMENT NUMBER: 137:190724
TITLE: Melanocortin metallopeptides for treatment of sexual dysfunction
INVENTOR(S): Sharma, Shubh D.; Shi, Yi-qun; Yang, Wei; Cai, Hui-zhi; Shadiack, Annette
PATENT ASSIGNEE(S): Palatin Technologies, Inc., USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002064091	A2	20020822	WO 2002-US4431	20020213
WO 2002064091	A3	20030313		

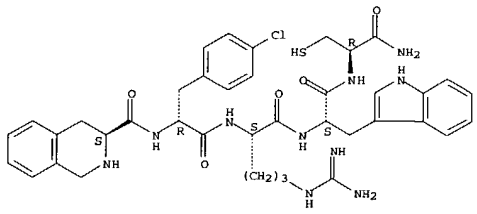
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004038897	A1	20040226	US 2003-640755	20030813
PRIORITY APPLN. INFO.:			US 2001-268591P	P 20010213
			WO 2002-US4431	A 20020213

OTHER SOURCE(S): MARPAT 137:190724
AB Metallopeptides are provided for use in treatment of sexual dysfunction in mammals. The metallopeptides are agonists for at least one of melanocortin-3 or melanocortin-4 receptors. The metallopeptides are conformationally fixed on complexation of a metal ion-binding portion thereof with a metal ion. Also provided are metallopeptides that are antagonists for at least one of melanocortin-3 or melanocortin-4 receptors.
IT **448903-51-3**
RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(melanocortin metallopeptides for treatment of sexual dysfunction)
RN 448903-51-3 CAPLUS
CN L-Cysteinamide, (3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-4-chloro-D-phenylalanyl-L-arginyl-L-tryptophyl- (9CI) (CA INDEX NAME)

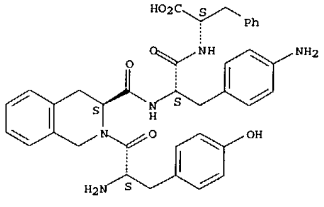
Absolute stereochemistry.

L4 ANSWER 59 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 60 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:576051 CAPLUS
DOCUMENT NUMBER: 137:279456
TITLE: Solid Phase Synthesis and Evaluation of Tyr-Tic-Phe-Phe(p-NHCOCH2Br) ([Phe(p-bromoacetamide)4]TIPP), a Potent Affinity Label for δ Opioid Receptors
AUTHOR(S): Kumar, Vivek; Murray, Thomas F.; Aldrich, Jane V.
CORPORATE SOURCE: Department of Pharmaceutical Sciences School of Pharmacy, University of Maryland, Baltimore, MD, 21201, USA
SOURCE: Journal of Medicinal Chemistry (2002), 45(18), 3820-3823
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Derivs. of the δ-opioid receptor-selective peptide H-Tyr-Tic-Phe-Phe-OH (TIPP) containing a p-bromoacetamide moiety on the Ph ring of Phe3 or Phe4 were prepared by solid-phase synthesis. [Phe(p-NHCOCH2Br)4]TIPP exhibited high affinity for cloned δ receptors (IC50 = 5.4 nM), and incubation with only 2.5 nM resulted in 85% wash resistant inhibition of radioligand binding to δ receptors. This peptide is a potent affinity label for further study of δ opioid receptors.
IT **320782-32-9P**
RL: BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(solid-phase preparation and δ-opioid receptor-binding affinity measurements of TIPP peptides with bromoacetamido groups)
RN 320782-32-9 CAPLUS
CN L-Phenylalanine, L-tyrosyl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-4-amino-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 61 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:575075 CAPLUS
DOCUMENT NUMBER: 137:140779
TITLE: Preparation of piperazine- and piperidine-derivatives as melanocortin receptor agonists
INVENTOR(S): Briner, Karin; Doecke, Christopher William; Mancoso, Vincent; Martinelli, Michael John; Richardson, Timothy Ivo; Rothhaar, Roger Ryan; Shi, Qing; Xie, Chaoyu
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 272 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002059117	A1	20020801	WO 2002-US515	20020123
WO 2002059117	C1	20031106		

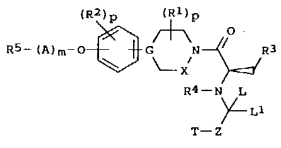
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

EP 1370558	A1	20031217	EP 2002-701922	20020123

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

PRIORITY APPLN. INFO.:	US 2001-263471P	P 20010123
	WO 2002-US515	W 20020123

OTHER SOURCE(S): MARPAT 137:140779
GI



I

AB The compds. of formula I (G = CR1, or N; A = alkyl, or cycloalkyl; L and L1 = H, or (together) oxo ; T = substituted indolyl, or pyrazinyl; X = CH2, or CH2CH2; Z = (CH2)n; R1 = H, alkyl, Ph, alkylaryl, alkylcarboxamide, cycloalkyl, or oxo; R2 = H, halo, alkyl, alkylsulfonyl, cycloalkyl, alkylaryl, or haloalkyl; R3 = (un)substituted aryl, or thienyl; R4 = H, alkyl, cycloalkyl, etc.; R5 = NH2, NPh2, alkylamide, alkylsulfonylamide, NHCOH, NHCONH2, NHSO2NH2, (un)substituted

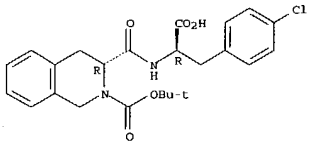
L4 ANSWER 61 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
heterocyclyl, etc.; n = 0-8, m = 0-1, and p = 0-4], pharmaceutically acceptable salts, or stereoisomers were prepd. as melanocortin receptor agonists for treatment of obesity, diabetes and male and/or female sexual dysfunction. Thus, coupling of 2-[(2-tert-butoxycarbonyl-1,2,3,4-tetrahydroisoquinolin-3-ylmethyl)amino]-3-(4-chlorophenyl)propionate with 3-(2-piperazin-1-yltrifluoromethylphenoxy)-S-pyrrolidine-1-carboxylic acid tert-Bu ester, followed by deprotection and addn. of HCl, gave 3-D-(4-chlorophenyl)-1-[4-(5-trifluoromethyl-2-S-(pyrrolidin-3-yloxy)phenyl]piperazin-1-yl]-2-D-[(1,2,3,4-tetrahydroisoquinoline-3-ylmethyl)amino]propan-1-one hydrochloride in 84% yield.

IT **252008-71-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperazine- and piperidine-derivs. as melanocortin receptor agonists for treatment of obesity, diabetes and sexual dysfunction)

RN 252008-71-2 CAPLUS

CN 2(1H)-Isoquinolinecarboxylic acid, 3-[[[(1R)-1-carboxy-2-(4-chlorophenyl)ethyl]amino]carbonyl]-3,4-dihydro-, 2-(1,1-dimethylethyl) ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



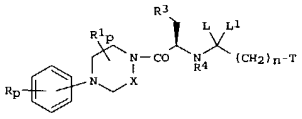
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 62 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:575066 CAPLUS
DOCUMENT NUMBER: 137:140777
TITLE: Preparation of piperazinyl and hexahydro-1,4-diazepinyl amino acid derivatives as melanocortin receptor agonists
INVENTOR(S): Biggers, Christopher Kelly; Briner, Karin; Doecke, Christopher William; Fisher, Matthew Joseph; Hertel, Larry Wayne; Mancoso, Vincent; Martinelli, Michael John; Mayer, John Philip; Ornstein, Paul Leslie; Richardson, Timothy Ivo; Shah, Jikesh Arvind; Shi, Qing; Wu, Zhipei; Xie, Chaoyu
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 356 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002059108	A1	20020801	WO 2002-US517	20020123
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1368340	A1	20031210	EP 2002-714719	20020123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2001-263471P P 20010123
WO 2002-US517 W 20020123
OTHER SOURCE(S): MARPAT 137:140777
GI



I

AB The invention relates to melanocortin receptor (MC-R) agonists I [X = CH2 or CH2CH2; LL1 = H2 or oxo; T = isoquinolinyl or tetrahydro derivative,

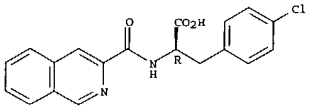
L4 ANSWER 62 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
isoindolinyl, or piperazinyl; n = 0-8; R = H, OH, CN, NO2, halo, alkyl, acyl, etc.; R1 = H, alkyl, alkylcarbamoyl, (D)phenyl, (D)cycloalkyl, or oxo (unless amide is formed); p = 0-5; R3 = (un)substituted aryl or thienyl; R4 = H, alkyl, acyl, cycloalkyl, or alkoxyalkyl], or their pharmaceutically-acceptable salts or stereoisomers, which are useful in the treatment of obesity, diabetes, and male and/or female sexual dysfunction. Compds. I comprise three domains, i.e., a piperazinyl or hexahydro-1,4-diazepinyl fragment, an amino acid, and a radical CLL1(CH2)n-T. Thus, 1-(D-Tic-4-Cl-D-Phe)-4-[2-(methanesulfonylamino)phenyl]piperazine (Tic = 1,2,3,4-tetrahydroisoquinoline-3-carbonyl; claimed compd.) was prepd. via acylation of the piperazine moiety.

IT **452330-88-0**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of piperazinyl and hexahydrodiazepinyl amino acid derivs. as melanocortin receptor agonists)

RN 452330-88-0 CAPLUS

CN D-Phenylalanine, 4-chloro-N-(3-isoquinolinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



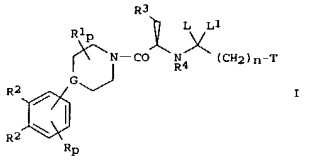
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 63 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:575065 CAPLUS
DOCUMENT NUMBER: 137:140776
TITLE: Preparation of piperidinyl and piperazinyl amino acid derivatives as melanocortin receptor agonists
INVENTOR(S): Backer, Ryan Thomas; Briner, Karin; Doecke, Christopher William; Fisher, Matthew Joseph; Kuklish, Steven Lee; Mancuso, Vincent; Martinelli, Michael John; Mullaney, Jeffrey Thomas; Xie, Chaoyu
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 263 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002059107	A1	20020801	WO 2002-US516	20020123
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1368339	A1	20031210	EP 2002-701923	20020123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2004058936	A1	20040325	US 2003-466249	20030711

PRIORITY APPLN. INFO.: US 2001-263595P P 20010123
WO 2002-US516 W 20020123
OTHER SOURCE(S): MARPAT 137:140776
GI



I

AB The invention relates to melanocortin receptor (MC-R) agonists I [G = CR1 or N; LL1 = H2 or oxo; T = isoquinolinyl or tetrahydro derivative, isoindolinyl, or piperazinyl; n = 0-8; R = H, OH, CN, NO2, halo, alkyl, acyl, etc.; R1 = H, alkyl, alkylcarbamoyl, (D)phenyl, (D)cycloalkyl, or oxo (unless amide is formed); p = 0-4; CR2CR2 is a 5- or 6-membered

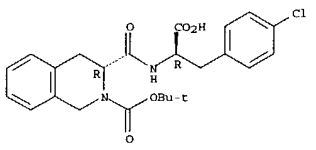
L4 ANSWER 63 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
carbocycle optionally substituted by 1-3 groups R; R3 = (un)substituted aryl or thienyl; R4 = H, alkyl, acyl, cycloalkyl, or alkoxyalkyl], or their pharmaceutically-acceptable salts or stereoisomers, which are useful in the treatment of obesity, diabetes, and male and/or female sexual dysfunction. Compds. I comprise three domains, i.e., a piperidino or piperazinyl fragment, an amino acid, and a radical CLL1(CH2)n-T. Thus, 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid [1-(4-chlorobenzyl)-2-[4-[2-(methylsulfonyl)-1,2,3,4-tetrahydroisoquinolin-8-yl]piperazin-1-yl]-2-oxoethyl]amide (claimed compd.) was prepd. via acylation of the piperazine moiety.

IT **252008-71-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperidinyl and piperazinyl amino acid derivs. as melanocortin receptor agonists)

RN 252008-71-2 CAPLUS

CN 2(1H)-Isoquinolinecarboxylic acid, 3-[[[(1R)-1-carboxy-2-(4-chlorophenyl)ethyl]amino]carbonyl]-3,4-dihydro-, 2-(1,1-dimethylethyl) ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



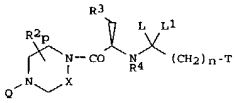
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 64 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:575055 CAPLUS
DOCUMENT NUMBER: 137:140775
TITLE: Preparation of piperazinyl and hexahydro-1,4-diazepinyl amino acid derivatives as melanocortin receptor agonists
INVENTOR(S): Backer, Ryan Thomas; Briner, Karin; Collado Cano, Ivan; De Frutos-Garica, Oscar; Doecke, Christopher William; Fisher, Matthew Joseph; Garcia-Paredes, Cristina; Kuklish, Steven Lee; Mancoso, Vincent; Martinelli, Michael John; Mateo Herranz, Ana Isabel; Mullaney, Jeffrey Thomas; Ornstein, Paul Leslie; Wu, Zhipei; Xie, Chaoyu
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 554 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002059095	A1	20020801	WO 2002-US518	20020123
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1358163	A1	20031105	EP 2002-701924	20020123
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.: US 2001-263380P P 20010123
WO 2002-US518 W 20020123
OTHER SOURCE(S): CASREACT 137:140775; MARPAT 137:140775
GI



I

AB The invention relates to melanocortin receptor (MC-R) agonists I [X = CH2 or CH2CH2; LL1 = H2 or oxo; R2 = H, alkyl, alkylcarbamoyl, (D)phenyl,

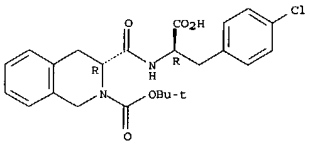
L4 ANSWER 64 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(D)cyclohexyl, or oxo if adjacent to N-Q; p = 0-4; R3 = (un)substituted Ph, aryl, or thienyl; R4 = H, alkyl, alkenyl, alkanoyl, or (D)phenyl; Q = various carbon-attached groups; T = isoquinolinyl or tetrahydro deriv., isoindolinyl, or piperazinyl; n = 0-8] which are useful in the treatment of obesity, diabetes, and male and/or female sexual dysfunction. Compds. I comprise three domains, i.e., a piperazinyl or hexahydro-1,4-diazepinyl fragment, an amino acid, and a radical CLL1(CH2)n-T. Thus, N-[1-(4-chlorobenzyl)-2-[4-[1-(cyclohexylmethyl)-2-morpholinoethyl]piperazin-1-yl]-2-oxoethyl]-2-(2,3-dihydro-1H-isoindol-1-yl)acetamide tris(trifluoroacetate) salt was prepd. via acylation of the piperazine moiety and showed EC50 = 69.3 nM in the MC-4 agonist assay.

IT **252008-71-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of piperazinyl and hexahydrodiazepinyl amino acid derivs. as melanocortin receptor agonists)

RN 252008-71-2 CAPLUS

CN 2(1H)-Isoquinolinecarboxylic acid, 3-[[[(1R)-1-carboxy-2-(4-chlorophenyl)ethyl]amino]carbonyl]-3,4-dihydro-, 2-(1,1-dimethylethyl) ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



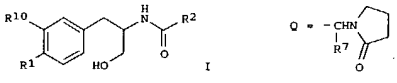
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 65 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:484863 CAPLUS
DOCUMENT NUMBER: 137:47448
TITLE: Preparation of substituted phenylalaninol derivatives as protein tyrosine phosphatase inhibitors
INVENTOR(S): Larsen, Scott D.; May, Paul D.; Bleasdale, John E.; Liljebris, Charlotta; Schostarez, Heinrich Josef; Barf, Tjeerd; Nilsson, Marianne
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 144 pp., Cont.-in-part of U.S. Ser. No. 138,642.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6410585	B1	20020625	US 1999-265410	19990310
US 6353023	B1	20020305	US 1998-138642	19980824
WO 2000053583	A1	20000914	WO 2000-US6022	20000309
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1161421	A1	20011212	EP 2000-917793	20000309
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002539115	T2	20021119	JP 2000-604023	20000309

PRIORITY APPLN. INFO.: US 1997-57730P P 19970828
US 1998-138642 A2 19980824
US 1999-265410 A 19990310
WO 2000-US6022 W 20000309
OTHER SOURCE(S): MARPAT 137:47448
GI



I

AB The invention comprises phenylalaninol deriva., e.g., I [R1 = OSO3H, OCH(CO2R5)2, OCH2CO2R5, OCH(CO2R5)CH2CO2R5, OC(CO2R5):CHCO2R5, CH2CH(CO2R5)2, CH:C(CO2R5)2, OCH2CONHOH, N(CH2CO2R5)2, OCHFCO2R5 (R5 = H, alkyl, alkylphenyl); R2 = CHR7NHXR6, group Q (R6 = alkyl, alkyl-CONH2, alkyl-NHCO2R5, etc.; R7 = H, any group given for R6); R10 = H, CO2R5, CONHOH, 5-tetrazolyl, F, OCH2CO2R5], or their pharmaceutically acceptable salts, as small mol. weight, non-peptidic inhibitors of protein tyrosine phosphatase 1 (PTP1) which are useful for the treatment and/or prevention of non-insulin dependent diabetes mellitus. Thus, 5-[(2S)-2-[[(2S)-2-

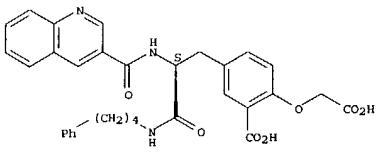
L4 ANSWER 65 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
[(tert-butoxycarbonyl)amino]-3-phenylpropanoyl]amino]-3-hydroxypropyl]-2-(carboxymethoxy)benzoic acid (claimed compd.) was prepd. and showed 80% inhibition of protein tyrosine phosphatase 1B at a concn. of 10 μM.

IT **292834-82-3P**
RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(preparation of substituted phenylalanine derivs. as protein tyrosine phosphatase inhibitors)

RN 292834-82-3 CAPLUS

CN Benzoic acid, 2-(carboxymethoxy)-5-[(2S)-3-oxo-3-[(4-phenylbutyl)amino]-2-[(3-quinolinylcarbonyl)amino]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 66 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:477236 CAPLUS

DOCUMENT NUMBER: 137:197780

TITLE: Molecular Imprinting for the Recognition of N-Terminal Histidine Peptides in Aqueous Solution

AUTHOR(S): Hart, Bradley R.; Shea, Kenneth J.

CORPORATE SOURCE: Department of Chemistry, University of California, Irvine, CA, 92697-2025, USA

SOURCE: Macromolecules (2002), 35(16), 6192-6201
CODEN: MAMOBX; ISSN: 0024-9297

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A new procedure for creating macromol. receptors for peptides using mol. imprinting has been developed. The polymeric receptor exhibits selective uptake of specific N-terminal histidine containing sequences of simple dipeptides. The polymerization and binding are carried out in water. The approach utilizes a strong Ni(II)-His binding to attract the N-terminus histidine of the dipeptide to the polymer surface and secondary interactions between peptide and polymer to discriminate between the peptide sequence. These developments are enabled by utilizing an aqueous based monomer formulation that includes N,N'-ethylenebis(acrylamide) as a water-soluble crosslinking monomer and a polymerizable NTA ligand, which can be used to incorporate nickel and other metals into these polyacrylamides. The Ni-NTA complex provides a strong histidine binding site that draws the dipeptide to the polymer surface. Mild polymerization conditions that utilize low concns. of water-soluble initiator and low-temperature result in quant. polymer yields. Variation of monomer composition reveals an optimum crosslinking for achieving maximum selectivity for these polymers.

IT **452928-69-7P**
RL: BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); PYP (Physical process); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(protocol for creating macromol. receptors for peptides using mol. imprinting with nickel-nitrilotriacetic acid complex)

RN 452928-69-7 CAPLUS

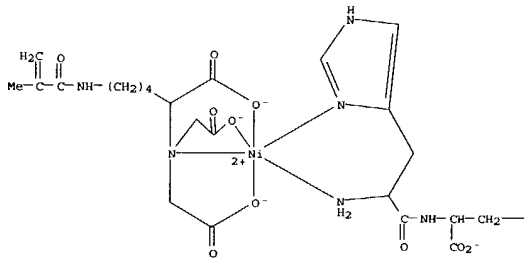
CN Nickelate(2-), [N2,N2-bis[(carboxy-κO)methyl]-N6-(2-methyl-1-oxo-2-propenyl)-L-lysinato(3-)-κN2,κO1](D-histidyl-κN,κN3-L-phenylalaninato)-, (OC-6-52)-, polymer with N,N'-1,2-ethanediylbis[2-propenamide] and 2-propenamide (9CI) (CA INDEX NAME)

CM 1

CRN 452928-68-6
CMF C29 H36 N6 Ni O10
CCI CCS

L4 ANSWER 66 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

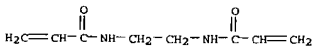


PAGE 1-B

— Ph

CM 2

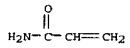
CRN 2956-58-3
CMF C8 H12 N2 O2



CM 3

L4 ANSWER 66 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

CRN 79-06-1
CMF C3 H5 N O



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 67 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:394477 CAPLUS
DOCUMENT NUMBER: 137:103998
TITLE: Structure-Activity Relationships of the Melanocortin Tetrapeptide Ac-His-DPhe-Arg-Trp-NH2 at the Mouse Melanocortin Receptors. 1. Modifications at the His Position
AUTHOR(S): Holder, Jerry Ryan; Bauzo, Rayna M.; Xiang, Zhimin; Haskell-Luevano, Carrie
CORPORATE SOURCE: Department of Medicinal Chemistry, University of Florida, Gainesville, FL, 32610, USA
SOURCE: Journal of Medicinal Chemistry (2002), 45(13), 2801-2810
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

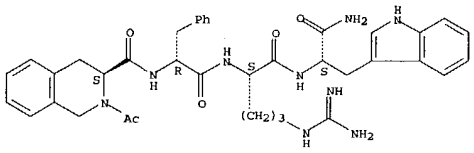
AB The melanocortin pathway is an important participant in obesity and energy homeostasis. The centrally located melanocortin-3 and melanocortin-4 receptors (MC3R, MC4R) are involved in the metabolic and food intake aspects of energy homeostasis and are stimulated by melanocortin agonists such as α-melanocyte stimulation hormone (α-MSH). The melanocortin agonists contain the putative message sequence "His-Phe-Arg-Trp", and it has been well documented that inversion of chirality of the Phe to DPhe results in a dramatic increase in melanocortin receptor potency. Herein, the authors report a tetrapeptide library based on the template Ac-His-DPhe-Arg-Trp-NH2, consisting of 17 members that have been modified at the His6 position (α-MSH numbering) and pharmacol. characterized for agonist activity at the mouse melanocortin receptors MC1R, MC3R, MC4R, and MC5R. These studies provide further exptl. evidence that the His6 position can determine MC4R vs. MC3R agonist selectivity and that chemical nonreactive side chains may be substituted for the imidazole ring (generally needs to be side chain protected in synthetic schemes) in the design of MC4R-selective, small-mol., non-peptide agonists. Specifically, the tetrapeptide containing the amino-2-naphthylcarboxylic acid (Anc) amino acid at the His position resulted in a potent agonist at the mMC4R (EC50 = 21 nM), was a weak mMC3R micromolar antagonist (pA2 = 5.6, Ki = 2.5 μM), and possessed >4700-fold agonist selectivity for the MC4R vs. the MC3R. Substitution of the His6 amino acid in the tetrapeptide template by the Phe, Anc, 3-(2-thienyl)alanine (2Thi), and 3-(4-pyridinyl)alanine (4-Pal) resulted in equipotency or only up to a 7-fold decrease in potency, compared to the His6-containing tetrapeptide at the mMC4R, demonstrating that these amino acid side chains may be substituted for the imidazole in the design of MC4R-selective non-peptide mols.

IT **443789-84-2P**
RL: BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(structure-activity relationships of melanocortin tetrapeptide analogs at mouse melanocortin receptors)

RN 443789-84-2 CAPLUS
CN L-Tryptophanamide, (3S)-2-acetyl-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-D-phenylalanyl-L-arginyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

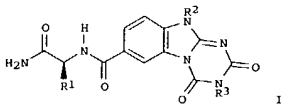
L4 ANSWER 67 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 68 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:392338 CAPLUS
DOCUMENT NUMBER: 137:140503
TITLE: Parallel Solid-Phase Synthesis of Trisubstituted Triazinobenzimidazolediones
AUTHOR(S): Klein, Gerard; Acharya, Achyuta N.; Ostresh, John M.; Houghten, Richard A.
CORPORATE SOURCE: Torrey Pines Institute for Molecular Studies, San Diego, CA, 92121, USA
SOURCE: Journal of Combinatorial Chemistry (2002), 4(4), 345-351
CODEN: JCCHFF; ISSN: 1520-4766
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:140503
GI



I

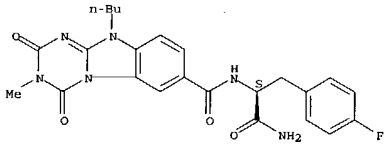
AB An efficient method for the solid-phase synthesis of trisubstituted [1,3,5]triazino[1,2-a]benzimidazole-2,4(3H,10H)-diones I (R1 = Me, Me2CHCH2, HOCH2, PhCH2, 4-FC6H4CH2; R2 = Bu, cyclopentyl, EtCHMe, etc.; R3 = Me, 4-FC6H4CH2, 3-MeC6H4CH2, 2,4-F2C6H3CH2, 3-MeOC6H4CH2) from resin-bound amino acids was developed. First, N-acylation of the primary amine of a resin-bound amino acid with 4-fluoro-3-nitrobenzoic acid, followed by displacement of the fluoro group with an amine and reduction of the nitro group, generated a resin-bound o-dianilino derivative The dianilino compound was treated with cyanogen bromide to generate the corresponding iminobenzimidazole, which, following treatment with N-(chlorocarbonyl)isocyanate, afforded the resin-bound triazinedione derivative Alkylation of the triazinedione compound with an alkyl halide following cleavage of the solid-support gave I.

IT **444813-51-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(parallel solid-phase synthesis of trisubstituted triazinobenzimidazolediones)

RN 444813-51-8 CAPLUS
CN 1,3,5-Triazino[1,2-a]benzimidazole-7-carboxamide, N-[(1S)-2-amino-1-[(4-fluorophenyl)methyl]-2-oxoethyl]-10-butyl-2,3,4,10-tetrahydro-3-methyl-2,4-dioxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 68 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

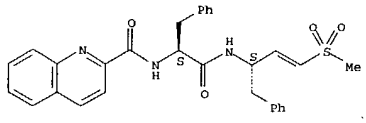
L4 ANSWER 69 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:378541 CAPLUS
DOCUMENT NUMBER: 136:386402
TITLE: Preparation of alkenylamino acids as proteasome inhibitors
INVENTOR(S): Kono, Yasushi; Ando, Naoki; Sawada, Takayuki; Kudo, Shinji; Kuriyama, Kazuhiko; Iwanami, Akira
PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 23 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002145848	A2	20020522	JP 2000-343930	20001110

PRIORITY APPLN. INFO.: JP 2000-343930 20001110
OTHER SOURCE(S): MARPAT 136:386402
AB A[NR1CHR2CO]mNHCHR3CONHCHR4CH:CR5R6 [A = Z, Boc, RCO, R(CO)2, RSO2; R = (un)substituted Ph, (un)substituted PhCH2, (un)substituted styryl, etc.; R1 = H; R1R2 may be linked to form pyrrolidine ring; R2-R4 = H, (un)substituted C1-4 alkyl, cyclohexylmethyl, (un)substituted PhCH2, etc.; R5 = H, F, C1-4 alkoxycarbonyl; R6 = C1-4 alkoxycarbonyl, CO2H, cyano, phenylsulfonyl, etc.; m = 0, 1], their pharmacol. acceptable salts, and their hydrates, useful as immunosuppressants, anti-inflammatory agents, antiallergy agents, anticancer agents, and nerve disorder-treating agents, are prepared by condensation of A[NR1CHR2CO]mNHCHR3CONHCHR4COH (A, R1-R4, m = same as above) with R7CHR8PO(OEt)2 (R7 = H, F; R8 = C1-4 alkoxycarbonyl, CO2H, C1-4 alkoxyphosphoryl, cyano, etc.) or R9CH2CO2Ra (R9 = C1-4 alkoxycarbonyl; Ra = C1-4 alkyl), followed by optional hydrolysis and further chemical modification. Thus, 150 mg MeSO2CH2PO(OEt)2 was treated with NaH in THF at room temperature for 1 h and condensed with 300 mg Z-L-Leu-L-Phe-L-Phe-H to give 89 mg Z-L-Leu-L-Phe-NH-L-CH(CH2Ph)CH:CHSO2Me, which inhibited proteasome with IC50 value of 0.14 μg/mL.
IT **428511-71-1P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of alkenylamino acids as proteasome inhibitors)
RN 428511-71-1 CAPLUS
CN 2-Quinolinecarboxamide, N-[(1S)-2-[[(1S)-3-(methylsulfonyl)-1-(phenylmethyl)-2-propenyl]amino]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

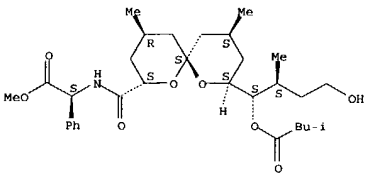
Absolute stereochemistry.
Double bond geometry unknown.

L4 ANSWER 69 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 70 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:312355 CAPLUS
DOCUMENT NUMBER: 137:63365
TITLE: Relative and Absolute Stereochemistry of the Didemnaketals, Metabolites of a Palauan Ascidian, Didemnum sp.
AUTHOR(S): Salomon, Christine E.; Williams, David H.; Lobkovsky, Emil; Clardy, Jon C.; Faulkner, D. John
CORPORATE SOURCE: Scripps Institution of Oceanography, UCSD, La Jolla, CA, 92093-0212, USA
SOURCE: Organic Letters (2002), 4(10), 1699-1702
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:63365
AB The absolute stereochem. of the heptaprenoids didemnaketals B and C, isolated from a Palauan ascidian, was determined using a combination of degradation and derivatization expts., chiral shift methods, and comparison of fragments to known compds.
IT **438462-64-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(isolation of didemnaketal C from Didemnum sp. and determination of relative and absolute configuration of didemnaketals B and C)
RN 438462-64-7 CAPLUS
CN Benzeneacetic acid, α-[[[(2S,4R,6S,8S,10S)-8-[(1S,2S)-4-hydroxy-2-methyl-1-(3-methyl-1-oxobutoxy)butyl]-4,10-dimethyl-1,7-dioxaspiro[5.5]undec-2-yl]carbonyl]amino]-, methyl ester, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 71 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:312037 CAPLUS
DOCUMENT NUMBER: 136:325436
TITLE: Preparation of quinolinylindoles as antimicrobial agents
INVENTOR(S): Cuny, Gregory D.; Hauske, James R.; Hoemann, Michael Z.; Chopra, Ian
PATENT ASSIGNEE(S): Sepracor Inc., USA
SOURCE: U.S., 167 pp., Cont. of U.S. Ser. No. 639,622.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

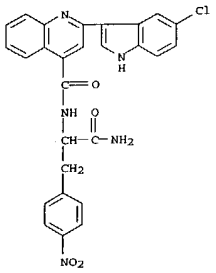
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6376670	B1	20020423	US 2000-658690	20000908
US 6207679	B1	20010327	US 1998-45051	19980319
US 6172084	B1	20010109	US 1998-99640	19980618
US 6103905	A	20000815	US 1998-213385	19981211

PRIORITY APPLN. INFO.: US 1997-878781 B2 19970619
US 1998-45051 A2 19980319
US 1998-99640 A2 19980618
US 1998-213385 A1 19981211
US 2000-639622 A2 20000815
OTHER SOURCE(S): MARPAT 136:325436
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; Z = CO, CR2; R = H, alkyl; R5-R8, R14-R17 = H, halo, alkyl, etc.; R9, R10 = H, alkyl, cycloalkyl, etc.; R3 = H, alkyl; R11 = H, alkyl; R12 = H, alkyl] which are bactericidal to a Gram-pos. bacterium via a non-lytic mechanism at its MIC (data given), were prepared E.g., a multi-step synthesis of II, was given.
IT **275357-08-9P**
RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation of quinolinylindole derivs. as antimicrobial agents)
RN 275357-08-9 CAPLUS
CN 4-Quinolinecarboxamide, N-[2-amino-1-[(4-nitrophenyl)methyl]-2-oxoethyl]-2-(5-chloro-1H-indol-3-yl)- (9CI) (CA INDEX NAME)

L4 ANSWER 71 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 72 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:293470 CAPLUS
DOCUMENT NUMBER: 136:319354
TITLE: Agents for the treatment of viral infections
INVENTOR(S): Schubert, Ulrich; Will, Hans; Tessmer, Uwe; Sirma, Huesseyin; Prassolow, Alexij; Schubert, Evelyn; Hohenberg, Heinz
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002030455	A2	20020418	WO 2001-DE3908	20011011
WO 2002030455	A3	20020808		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10051716	A1	20020425	DE 2000-10051716	20001012
DE 10149398	A1	20030424	DE 2001-10149398	20011003
AU 2002018133	A5	20020422	AU 2002-18133	20011011
EP 1326632	A2	20030716	EP 2001-986607	20011011
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004510826	T2	20040408	JP 2002-533894	20011011

PRIORITY APPLN. INFO.: DE 2000-10051716 A 20001012
DE 2001-10149398 A 20011003
WO 2001-DE3908 W 20011011

AB The invention relates to agents for the treatment of viral infections, in particular, infections with hepatitis and retroviruses. Said agents inhibit the release, maturation and replication of both retroviruses and also hepatitis viruses. In the example of human immune deficiency virus (HIV) and hepatitis-B viruses it has been shown that proteasome inhibitors block the release of virus particles and the infectiousness of the released viral particles and thus the reproduction of the viruses. The proteasome inhibitors affect the activities in the ubiquitin/proteasome pathway, in particular the enzymic activities of the 26S and the 20S proteasome complexes. The application for the above invention lies in antiretroviral therapy, particularly the treatment of HIV infections and AIDS and in the antiviral therapy of hepatitis infections, in particular the treatment of acute and chronic HBV and HCV infections and the associated liver carcinomas.

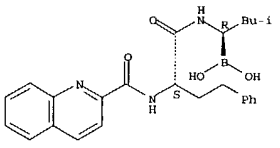
IT **179324-59-5**, PS 325
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(proteasome-inhibitory agents for treatment of viral infections)

RN 179324-59-5 CAPLUS

L4 ANSWER 72 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

CN Boronic acid, [(1R)-3-methyl-1-[[(2S)-1-oxo-4-phenyl-2-[(2-quinolinylcarbonyl)amino]butyl]amino]butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 73 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:256223 CAPLUS
DOCUMENT NUMBER: 136:295089
TITLE: Preparation of amino acid aromatic derivatives with HIV integrase inhibitory properties
INVENTOR(S): N'zemba, Blaise Magloire; Sauve, Gilles; Sevigny, Guy; Yelle, Jocelyn
PATENT ASSIGNEE(S): Pharmacor, Inc., Can.
SOURCE: PCT Int. Appl., 173 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002026697	A2	20020404	WO 2001-CA1367	20010925
WO 2002026697	A3	20020516		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001095310	A5	20020408	AU 2001-95310	20010925
US 6528655	B1	20030304	US 2001-963329	20010926

PRIORITY APPLN. INFO.: CA 2000-2321348 A 20000927
WO 2001-CA1367 W 20010925

OTHER SOURCE(S): MARPAT 136:295089

AB Amino acid derivs. R1CO-A-CONHR2 [A = NR3CR4R5, where R3, R4 = H or Me; R5 = H, alkyl, carboxyalkyl, benzyl, MeSCH2CH2, 1-indolylmethyl, 3,4-(HO)2C6H2CH2, etc.; R3R4 may be trimethylene, which may be substituted; R1, R2 are certain rings (Ph, 3-pyridyl, 2-quinolyl, 2-thienyl, etc.), which may be substituted and attached to alkyl; R2 may also be aroylamino] were prepared as inhibitors of HIV integrase. Thus, N-[Nα-(3,4-dihydroxybenzoyl)-Nτ-trityl-L-histidinyl]dopamine was prepared by coupling of Nα-(9-fluorenylmethoxycarbonyl)-Nτ-trityl-L-histidine with dopamine hydrochloride, deprotection, and acylation with 3,4-dihydroxybenzoic acid and showed anti-integrase activity IC50 = 65 nM.

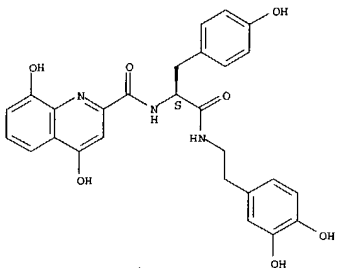
IT **406728-01-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid aromatic derivs. with HIV integrase inhibitory properties)

RN 406728-01-6 CAPLUS

CN 2-Quinolinecarboxamide, N-[(1S)-2-[[2-(3,4-dihydroxyphenyl)ethyl]amino]-1-[(4-hydroxyphenyl)methyl]-2-oxoethyl]-4,8-dihydroxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 73 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 74 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:252956 CAPLUS
DOCUMENT NUMBER: 136:273215
TITLE: Combination of an NK-3 receptor antagonist and a CNS-penetrant NK-1 receptor antagonist for treating depression and anxiety
INVENTOR(S): Lowe, John Adams, III; McLean, Stafford; Sobolov-Jaynes, Susan Beth
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 65 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

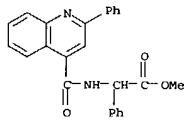
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1192952	A2	20020403	EP 2001-307657	20010910
EP 1192952	A3	20030326		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2001004345	A	20020521	BR 2001-4345	20010928
JP 2002338497	A2	20021127	JP 2001-300136	20010928

PRIORITY APPLN. INFO.: US 2000-236375P P 20000928
OTHER SOURCE(S): MARPAT 136:273215

AB A composition for the treatment of anxiety or depression in a mammal, including a human, comprises (a) an NK-3 receptor antagonist or its salt, (b) a CNS-penetrant NK-1 receptor antagonist or its salt, and (c) a pharmaceutically acceptable carrier. When administered in combination, either as a single or as sep. pharmaceutical composition(s), the CNS-penetrant NK-1 receptor antagonist and an NK-3 antagonist, are presented in a ratio which is consistent with the manifestation of the desired effect. In particular, the ratio by weight of the CNS-penetrant NK-1 receptor antagonist and the NK-3 antagonist will suitably be between 0.001:1 to 1000:1, and especially between 0.01:1 and 100:1.

IT **174635-51-9**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination of NK3 receptor antagonist and CNS-penetrant NK1 receptor antagonist for treating depression and anxiety)

RN 174635-51-9 CAPLUS
CN Benzeneacetic acid, α-[[(2-phenyl-4-quinolinyl)carbonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)

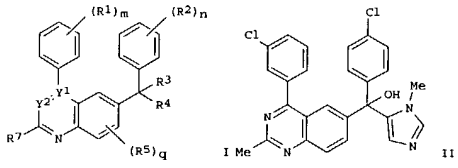


L4 ANSWER 75 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:240759 CAPLUS
DOCUMENT NUMBER: 136:279469
TITLE: Preparation of quinoline and quinazoline derivatives as farnesyl transferase inhibitors for treatment of tumors and proliferative diseases
INVENTOR(S): Angibaud, Patrick Rene; Venet, Marc Gaston; Pilatte, Isabelle Noeelle Constance
PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002024682	A1	20020328	WO 2001-EP10867	20010918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1322635	A1	20030702	EP 2001-974271	20010918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004509883	T2	20040402	JP 2002-529092	20010918
AU 2001093826	A5	20020402	AU 2001-93826	20020402
US 2003203904	A1	20031030	US 2003-381363	20030324

PRIORITY APPLN. INFO.: EP 2000-203365 A 20000925
WO 2001-EP10867 W 20010918
OTHER SOURCE(S): MARPAT 136:279469
GI



I Me II

AB Title compds. I [wherein m and n = independently 0-5; q = 0-3; Y1Y2 = C:N or C:CR9; C9 = H, halo, CN, (cyclo)alkyl, hydroxyalkyl, alkoxy(alkyl), aminoalkyl, (amino)alkenyl, (amino)alkynyl, halocarbonyl, hydroxycarbonyl, alkoxycarbonyl, aryl, (un)substituted amino or carbamoyl, etc.; R1 and R2= independently azido, OH, halo, CN, NO2, trihalomethyl, alkoxy, aryloxy,

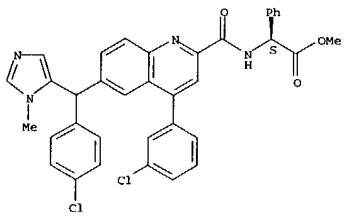
L4 ANSWER 75 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

heterocyclyloxy, alkylthio, or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, carbamoyl, amino, sulfamoyl, etc.; or R1R2 = OCH2O, OCH2CH2O, OCH:CH, OCH2CH2, OCH2CH2CH2, CH:CHCH:CH; R3 = H, halo, CN, alkenyl, alkynyl, hydroxycarbonyl, alkoxycarbonyl, aryl, heterocyclyl, alkoxy, alkylthio, (un)substituted (cyclo)alkyl or amino, etc.; R4 = (un)substituted imidazolyl, triazolyl, or pyridyl; R5 = CN, OH, halo, alkenyl, alkynyl, hydroxycarbonyl, alkoxycarbonyl, or (un)substituted (cyclo)alkyl, alkoxy, amino, or carbamoyl, etc.; R7 = halo or (un)substituted (cyclo)alkyl, alkenyl, alkynyl, alkylthio, carboxy, carbamoyl, acyl(amino), etc.; or pharmaceutically acceptable salts, N-oxides, or stereochem. isomeric forms thereof] were prepd. For example, N-[2-(3-chlorobenzoyl)-4-(4-chlorobenzoyl)phenyl]acetamide was cyclized with NH3 in i-PrOH to give (4-chlorophenyl){4-(3-chlorophenyl)-2-methyl-6-quinazolinyl]methanone (36%). Addn. of 1-methyl-1H-imidazole in the presence of BuLi and SiEt3Cl in THF afforded II (40%). I have potent farnesyl transferase inhibitory effect and are useful for inhibiting proliferative diseases and growth of tumors expressing an activated ras oncogene (no data).

IT **405549-73-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(farnesyl transferase inhibitor; preparation of quinoline and quinazoline derivs. as farnesyl transferase inhibitors for treatment of tumors and proliferative diseases)

RN 405549-73-7 CAPLUS
CN Benzeneacetic acid, α-[[[4-(3-chlorophenyl)-6-[(4-chlorophenyl)(1-methyl-1H-imidazol-5-yl)methyl]-2-quinolinyl]carbonyl]amino]-, methyl ester, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

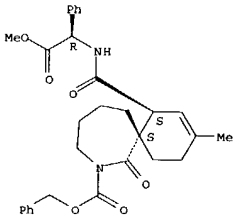
L4 ANSWER 76 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:209379 CAPLUS
DOCUMENT NUMBER: 137:33156
TITLE: Asymmetric construction of the azaspiro[5.6]dodec-9-ene system in marine natural toxins
AUTHOR(S): Ishihara, Jun; Horie, Mariko; Shimada, Yoshikatsu; Tojo, Shingo; Murai, Akio
CORPORATE SOURCE: Division of Chemistry, Graduate School of Science, Hokkaido University, Sapporo, 060-0810, Japan
SOURCE: Synlett (2002), (3), 403-406
CODEN: SYNLES; ISSN: 0936-5214
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:33156

AB The asym. formation of azaspiro[5.6]dodec-9-ene system is described. The Diels-Alder reactions of an α-methylene caprolactam and diene in the presence of a Cu(II) and (S,S)-tert-Bu-BOX complex afford the desired spirocyclic compds. with good exo-selectivity as well as excellent enantioselectivity. These exo-adducts would be applicable to the synthesis of marine natural toxins including the corresponding cyclic imine moiety.

IT **436153-34-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(asym. synthesis of azaspiro[5.6]dodec-9-ene system in marine natural toxins via copper-catalyzed stereoselective Diels-Alder reaction)

RN 436153-34-3 CAPLUS
CN 8-Azaspiro[5.6]dodec-2-ene-8-carboxylic acid, 1-[[[(1R)-2-methoxy-2-oxo-1-phenylethyl]amino]carbonyl]-3-methyl-7-oxo-, phenylmethyl ester, (1S,6S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 77 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:209378 CAPLUS
DOCUMENT NUMBER: 137:78803
TITLE: Asymmetric construction of the azaspiro[5.5]undec-8-ene system towards gymnodimine synthesis
AUTHOR(S): Tsujimoto, Takashi; Ishihara, Jun; Horie, Mariko; Murai, Akio
CORPORATE SOURCE: Division of Chemistry, Graduate School of Science, Hokkaido University, Sapporo, 060-0810, Japan
SOURCE: Synlett (2002), (3), 399-402
CODEN: SYNLES; ISSN: 0936-5214
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 137:78803
GI

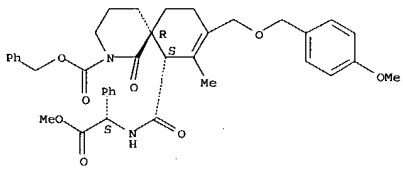
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB In the course of the synthetic studies on gymnodimine (I), a potent shellfish toxin, the asym. construction of the azaspiracyclic part II was achieved by the (-)-siam-Cu(SbF6)2 complex catalyzed intermol. Diels-Alder reaction in high exo- and enantioselectivities.

IT **440677-28-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(asym. construction of the azaspiro[5.5]undec-8-ene system towards gymnodimine synthesis)

RN 440677-28-1 CAPLUS
CN 2-Azaspiro[5.5]undec-8-ene-2-carboxylic acid, 7-[[[(1S)-2-methoxy-2-oxo-1-phenylethyl]amino]carbonyl]-9-[[(4-methoxyphenyl)methoxy]methyl]-8-methyl-1-oxo-, phenylmethyl ester, (6R,7S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



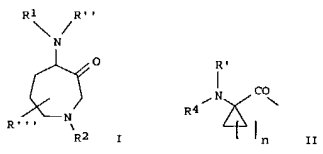
REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 78 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:171694 CAPLUS
DOCUMENT NUMBER: 136:232208
TITLE: Preparation of 4-aminoazepan-3-one parasitic cysteine protease inhibitors effective against malaria and other diseases
INVENTOR(S): Tew, David G.; Thompson, Scott K.; Veber, Daniel F.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, UK
SOURCE: PCT Int. Appl., 220 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002017924	A1	20020307	WO 2001-US27178	20010831
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003144175	A1	20030731	US 2001-881334	20010614
AU 2001086983	A5	20020313	AU 2001-86983	20010831
EP 1320370	A1	20030625	EP 2001-966474	20010831
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004509083	T2	20040325	JP 2002-522897	20010831

PRIORITY APPLN. INFO.:
US 2000-653815 A2 20000901
US 2001-881334 A2 20010614
US 1998-113636P P 19981223
US 1999-164581P P 19991110
WO 1999-US30730 A2 19991221
US 2000-593845 B2 20000614
WO 2001-US27178 W 20010831

OTHER SOURCE(S): MARPAT 136:232208
GI



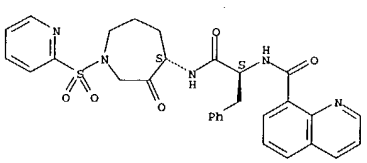
AB The present invention relates to methods of treating parasitic diseases which are mediated by cysteine proteases by administration of 4-aminoazepan-3-one protease inhibitors I (e.g. benzo[1,3]dioxole-5-carboxylic acid [(S)-1-(1-benzyl-3-oxoazepan-4-ylcarbamoyl)-3-

L4 ANSWER 78 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
methylbutyl]amide) and pharmaceutically acceptable salts, hydrates and solvates thereof. In particular, the present invention relates to a method of treating malaria by inhibiting the cysteine protease falcipain. Other diseases against which the claimed compds. are effective include trypanosomiasis (African sleeping sickness, Chagas disease), leishmaniasis, schistosomiasis, onchocerciasis (river blindness) and giardiasis. In I: R1 is R4NR'CHR3C(O)-, R5XCHR3C(O)-, R3CH2C(O)-, R4NR'CR''''R3C(O)-, II. R2 is H, C1-6alkyl, C3-6cycloalkyl-C0-6alkyl, Ar-C0-6alkyl, Het-C0-6alkyl, R9C(O)-, R9C(S)-, R9SO2-, R9OC(O)-, R9R11NC(O)-, R9R11NC(S)-, R9(R11)NSO2-, 3-(2-pyridyl)benzylcarbonyl, 2-(3-(2-pyridyl)phenyl)ethyl, R7NR6CHR8Z-, and R9SO2R11NC(O)-. R3 is H, C1-6alkyl, C3-6cycloalkyl-C0-6alkyl, C2-6alkenyl, C2-6alkynyl, HetC0-6alkyl and ArC0-6alkyl. R3 and R' may be connected to form a pyrrolidine, piperidine or morpholine ring. R4 is H, C1-6alkyl, C3-6cycloalkyl-C0-6alkyl, Ar-C0-6alkyl, Het-C0-6alkyl, R5C(O)-, R5C(S)-, R5SO2-, R5OC(O)-, R5R12NC(O)-, and R5R12NC(S)-. R5 is H, C1-6alkyl, C2-6alkenyl, C2-6alkynyl, C3-6cycloalkyl-C0-6alkyl, Ar-C0-6alkyl and Het-C0-6alkyl. R6 is H, C1-6alkyl, Ar-C0-6alkyl, and Het-C0-6alkyl. R7 is H, C1-6alkyl, C3-6cycloalkyl-C0-6alkyl, Ar-C0-6alkyl, Het-C0-6alkyl, R10C(O)-, R10C(S)-, R10SO2-, R10OC(O)-, R10R13NC(O)-, and R10R13NC(S)-. R8 is H, C1-6alkyl, C2-6alkenyl, C2-6alkynyl, HetC0-6alkyl and ArC0-6alkyl. R9, R10 independently = C1-6alkyl, C3-6cycloalkyl-C0-6alkyl, Ar-C0-6alkyl and Het-C0-6alkyl. R11, R12, R13, R', R'' independently = H, C1-6alkyl, Ar-C0-6alkyl, and Het-C0-6alkyl. R''' is H, C1-6alkyl, C3-6cycloalkyl-C0-6alkyl, Ar-C0-6alkyl, and Het-C0-6alkyl; R'''' is C1-6alkyl, C3-6cycloalkyl-C0-6alkyl C2-6alkenyl, C2-6alkynyl, HetC0-6alkyl and ArC0-6alkyl. X is CH2, S, and O; Z is C(O) and CH2; n is 1-5. Although the methods of prepn. are not claimed, 220 example prepns. are included.

IT **350796-41-7P**, Quinoline-8-carboxylic acid [(1S)-1-[[(4S)-3-oxo-1-(pyridin-2-ylsulfonyl)azepan-4-yl]carbamoyl]-2-phenylethyl]amide
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-aminoazepan-3-one parasitic cysteine protease inhibitors effective against malaria and other diseases)

RN 350796-41-7 CAPLUS
CN 8-Quinolinecarboxamide, N-[(1S)-2-[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-2-oxo-1-(phenylmethyl)ethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

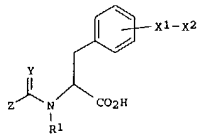


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 79 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:142667 CAPLUS
DOCUMENT NUMBER: 136:200103
TITLE: Preparation of (thio)urea moiety-containing heterocyclic compounds as VLA-4 antagonists
INVENTOR(S): Fukui, Hideto; Ikegami, Satoru; Okuyama, Akihiko
PATENT ASSIGNEE(S): Kaken Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002014272	A1	20020221	WO 2001-JP6833	20010808
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001077720	A5	20020225	AU 2001-77720	20010808
PRIORITY APPLN. INFO.:			JP 2000-241657 A	20000809
			WO 2001-JP6833 W	20010808

OTHER SOURCE(S): MARPAT 136:200103
GI

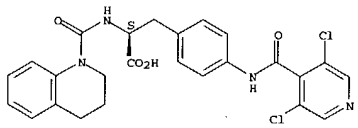


I

AB The title compds. I [R1 = H, alkyl, etc.; X1 = single bond, C.tplbond.C, etc.; Y = O, etc.; Z = NR7R8, etc.; R7, R8 = H, hydrocarbon, etc.; X2 = heterocyclic ring (generic structure given); further details on said heterocyclic ring are given] are prepared A process for the preparation of I is claimed. In an assay for inhibition of VLA-4/VCAM-1 adhesion, 3-[4-[(3,5-dichloropyridine-4-carbonyl)amino]phenyl]-2-(S)-[3-isobutyl-3-[1(S)-phenylethyl]ureido]propionic acid showed IC50 of 1.1 nM.
IT **401470-80-2P**

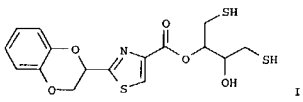
L4 ANSWER 79 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of (thio)urea moiety-contg. heterocyclic compds. as VLA-4 antagonists)
RN 401470-80-2 CAPLUS
CN L-Phenylalanine, 4-[[(3,5-dichloro-4-pyridinyl)carbonyl]amino]-N-[(3,4-dihydro-1(2H)-quinolinyl)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 80 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:116963 CAPLUS
DOCUMENT NUMBER: 137:163311
TITLE: A new class of type I protein geranylgeranyltransferase (GGTase I) inhibitor
AUTHOR(S): Sunami, Satoshi; Ohkubo, Mitsuru; Sagara, Takeshi; Ono, Jun; Asahi, Shuichi; Koito, Seita; Morishima, Hajime
CORPORATE SOURCE: Banyu Tsukuba Research Institute, Ibaraki, Tsukuba, 300-2611, Japan
SOURCE: Bioorganic & Medicinal Chemistry Letters (2002), 12(4), 629-632
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

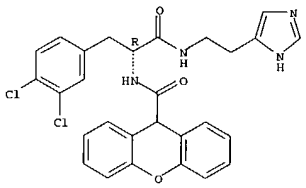


I

AB Replacement of the thiol groups in I, a potent and highly selective Candida albicans GGTase I inhibitor discovered through screening, with an imidazole ring was achieved by using solid phase synthesis. A non-thiol compound was found as a representative of a new class of potent C. albicans GGTase I inhibitor with high selectivity against human GGTase I. The relation of these results to the possible antifungal activity of these compds. is discussed.
IT **445400-99-7P**
RL: CPN (Combinatorial preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); CMBI (Combinatorial study); PREP (Preparation); USES (Uses)
(new class of type I protein geranylgeranyltransferase (GGTase I) inhibitor in relation to structure and antifungal activity)
RN 445400-99-7 CAPLUS
CN 9H-Xanthene-9-carboxamide, N-[(1R)-1-[(3,4-dichlorophenyl)methyl]-2-[[2-(1H-imidazol-4-yl)ethyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 80 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 81 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:107157 CAPLUS
DOCUMENT NUMBER: 136:167388
TITLE: Preparation and use of quinolone and naphthyridine derivatives as inhibitors of cellular efflux pumps of microbes
INVENTOR(S): De Souza, Noel J.; Patel, Mahesh V.; Gupta, Shrikant V.; Upadhyay, Dilip J.; Shukla, Milind C.; Chaturvedi, Nishith C.; Bhawsar, Satish B.; Nair, Sheela C.; Jafri, Mohammed A.; Khorakiwala, Habil F.
PATENT ASSIGNEE(S): Wockhardt Limited, India
SOURCE: PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002009758	A2	20020207	WO 2001-IN139	20010731
WO 2002009758	A3	20021227		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002165227	A1	20021107	US 2001-850669	20010507
US 6608078	B2	20030819		
AU 2001080091	A5	20020213	AU 2001-80091	20010731
US 2002177559	A1	20021128	US 2001-919347	20010731
EP 1305048	A2	20030502	EP 2001-958373	20010731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
US 2003144517	A1	20030731	US 2002-303692	20021122

PRIORITY APPLN. INFO.:
US 2000-222201P P 20000801
US 2000-640947 A 20000819
WO 2000-IN111 W 20001121
US 2001-286291P P 20010425
US 2001-850669 A 20010507
WO 2001-IN100 A 20010508
US 1999-170676P P 19991214
US 2000-202459P P 20000508
US 2000-566875 A2 20000508
US 2001-802793 A3 20010309
WO 2001-IN139 W 20010731

OTHER SOURCE(S): MARPAT 136:167388
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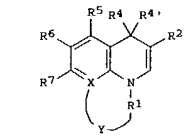
L4 ANSWER 81 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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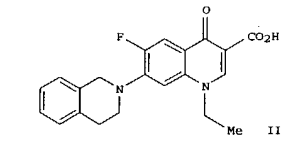


II

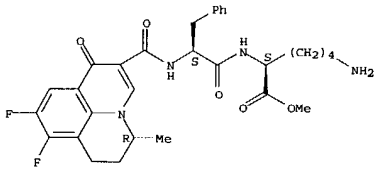
AB Title compds. I [R1 = H, (cyclo)alkyl, aryl, aralkyl, arylaminoalkyl, aryloxyalkyl, arylSO0-2 alkyl or when X = C and the nitrogen atom to which R1 is linked forms an (un)substituted 4-7 membered ring with X of the adjacent ring, the ring optionally containing one or more hetero atoms selected from N, O, S, said heteroatom(s) represented by Y; R2 = H, CHO, COOR3, CONHR13, where R13 = H or the NHR13 of CONHR13 is the residue of an amino acid; R3 = H, alkyl, cycloalkyl, aryl, aralkyl, arylaminoalkyl, aryloxyalkyl, arylSO0-2 alkyl, O-carboxy, etc.; R4 = H; R4' = H or R4 and R4' taken together are :O, :S; R5 = H, alkyl, amino, alkylamino, acylamino; R6 = H, alkyl, halo, amino, hydroxy; R7 = OH, halo, NR9R10, etc.; R9-10 = H, alkyl, (CH2)nOA or R9 = H and R10 = 4-7 membered carbocyclic, heterocyclic ring linked to the nitrogen of NR9R10 through an atom of the heterocycle other than the heterocyclic atom, etc.; A = H, alkyl, glycosyl, aralkyl, alkanoyl, aminoalkanoyl wherein the aminoalkanoyl group may be an amino acid residue or A is C6H11O6, SO3H, PO3H2; X = CH, CF, CCl, CCH3, CCF3, COCH3, COCHF2, C-OCF3, N or when X is equal to C it forms together with the nitrogen atom of the adjacent ring an (un)substituted 5-7 membered ring containing carbon atoms and optionally Y atoms representing one or more N, O, S] were prepared For instance, a mixture of 1-ethyl-6,7-difluoro-1,4-dihydro-4-oxoquinolone-3-carboxylic acid and 1,2,3,4-tetrahydroisoquinoline (DMSO, Et3N 140°C, 24 h) provided, after work-up and trituration II as a solid (62% yield), m.p. 220°C. II with ciprofloxacin had a fractional inhibitory concentration (FIC) index of 0.314 observed against S. aureus 1199 B (Nor A+). I are effective at inhibiting efflux pumps, e.g., MefA, MefE, Bmr, PmrA, etc.

IT **396132-84-6P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; preparation and use of quinolone and naphthyridine derivs. as inhibitors of cellular efflux pumps of microbes)

L4 ANSWER 81 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

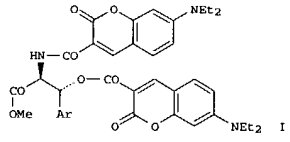
RN 396132-84-6 CAPLUS
CN L-Lysine, N-[[(5R)-8,9-difluoro-6,7-dihydro-5-methyl-1-oxo-1H,5H-benzo[ij]quinolizin-2-yl]carbonyl]-L-phenylalanyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L4 ANSWER 82 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:73778 CAPLUS
DOCUMENT NUMBER: 136:279671
TITLE: A CD Exciton Chirality Method for Determination of the Absolute Configuration of threo-β-Aryl-β-hydroxy-α-amino Acid Derivatives
AUTHOR(S): Lo, Lee-Chiang; Yang, Chun-Tzu; Tsai, Charng-Sheng
CORPORATE SOURCE: Department of Chemistry, National Taiwan University, Taipei, 106, Taiwan
SOURCE: Journal of Organic Chemistry (2002), 67(4), 1368-1371
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:279671
GI



I

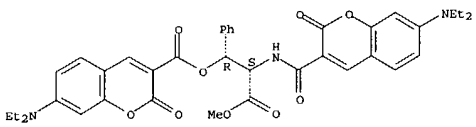
AB Threo-β-aryl-β-hydroxy-α-amino acids I (Ar = Ph, C6H4CN-4, C6H4NO2-3, C6H4NO2-2, C6H4Cl-3, C6H4OMe-2, 2,5-dimethoxyphenyl, 2,4-dimethylphenyl) were prepared and their absolute configuration was studied in CH2Cl2 by CD exciton chirality method using 7-diethylaminocoumarin-3-carboxylate as a red-shifted chromophore. By combining the data of CD and NMR coupling consts., the authors were able to correlate the preferred conformer (B) and the pos. CD to the corresponding (2S,3R)-absolute configuration. These results are consistent with those obtained from serine and threonine derivs., which represent the simplest form of β-hydroxy-α-amino acids. Thus, this CD method could become a general method for determining the absolute configuration of threo-β-aryl-β-hydroxy-α-amino acids.

IT **405510-93-2P**
RL: BPN (Biosynthetic preparation); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(CD exciton chirality method for determining absolute configuration of chromophore-containing β-aryl-β-hydroxy amino acid esters)

RN 405510-93-2 CAPLUS
CN 2H-1-Benzopyran-3-carboxylic acid, 7-(diethylamino)-2-oxo-, (1R,2S)-2-[[[7-(diethylamino)-2-oxo-2H-1-benzopyran-3-yl]carbonyl]amino]-3-methoxy-3-oxo-1-phenylpropyl ester (9CI) (CA INDEX NAME)

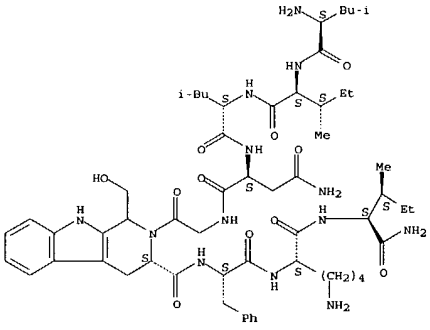
Absolute stereochemistry.

L4 ANSWER 82 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 83 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 83 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2002:46807 CAPLUS
DOCUMENT NUMBER: 137:185793
TITLE: Constrained segment ligation
AUTHOR(S): Tam, James P.; Miao, Zhenwei
CORPORATE SOURCE: Department of Microbiology and Immunology, Vanderbilt University, Nashville, TN, 37232-2363, USA
SOURCE: Innovation and Perspectives in Solid Phase Synthesis & Combinatorial Libraries: Peptides, Proteins and Nucleic Acids--Small Molecule Organic Chemistry Diversity, Collected Papers, International Symposium, 6th, York, United Kingdom, Aug. 31-Sept. 4, 1999 (2001), Meeting Date 1999, 11-14. Editor(s): Epton, Roger. Mayflower Scientific Ltd.: Kingswinford, UK.
CODEN: 69CEGV; ISBN: 0-9515735-3-5
DOCUMENT TYPE: Conference
LANGUAGE: English

AB A symposium report. Imine ligation of Leu-Ile-Leu-Asn-Gly-OCH2CHO with N-terminal (NT) amino acids in pyridine-acetic acid mixts. is highly regiospecific. Oxaprolines from NT-Ser and NT-Thr as well as thiaprolines from NT-Cys are useful pseudoprolines (Ψpro). Differences in ligation rates are useful for an orthogonal tandem ligation strategy to couple multiple unprotected peptide segments without a protection scheme. Model dipeptides were used to study the stereochem. of the Ψpro derived from imine ligation.

IT **451524-16-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(ligation of peptide glycoaldehyde esters with N-terminal peptides)

RN 451524-16-6 CAPLUS

CN L-Isoleucinamide, L-leucyl-L-isoleucyl-L-leucyl-L-asparaginylglycyl-(3S)-2,3,4,9-tetrahydro-1-(hydroxymethyl)-1H-pyrido[3,4-b]indole-3-carbonyl-L-phenylalanyl-L-lysyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 84 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

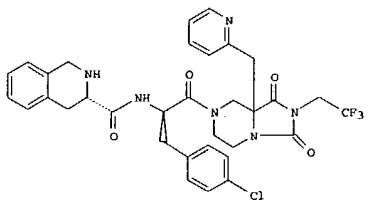
ACCESSION NUMBER: 2002:10473 CAPLUS
DOCUMENT NUMBER: 136:69824
TITLE: Preparation of heterocycle compounds as melanocortin receptor ligands
INVENTOR(S): Carpino, Philip Albert; Cole, Bridget McCarthy; Morgan, Bradley Paul
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: PCT Int. Appl., 108 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000654	A1	20020103	WO 2001-IB995	20010531
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1294719	A1	20030326	EP 2001-934254	20010531
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001011567	A	20030506	BR 2001-11567	20010531
JP 2004501917	T2	20040122	JP 2002-505778	20010531
US 2002072604	A1	20020613	US 2001-891026	20010625
BG 107268	A	20030630	BG 2002-107268	20021112
NO 2002006280	A	20021230	NO 2002-6280	20021230

PRIORITY APPLN. INFO.: US 2000-214616P P 20000628
WO 2001-IB995 W 20010531

OTHER SOURCE(S): MARPAT 136:69824

GI



II

AB Compds. represented by formula HET-COCR3R4-NX4-CO(CR6R7)m-D [I; wherein m = 0, 1 or 2; HET = heterocyclyl; R3, R4 = H,, C1-8 alkyl, CH(R8)-aryl, -CH(R8)-heteroaryl, -C0-3 alkyl-C3-8 cycloalkyl (wherein the aryl or

L4 ANSWER 84 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
heteroaryl groups are optionally substituted by one or two groups; R8 = H, C1-8 alkyl, -C0-3 alkylaryl, -C0-3 alkylheteroaryl, -C3-6 cycloalkyl); R6, R7 = H, C1-6 alkyl, -C0-3 alkyl-aryl, -C0-3 alkyl-heteroaryl, -C0-3 alkyl-C3-8 cycloalkyl; or R6 and R7 together with the nitrogen atom to which they are attached form a 5- or 6-membered ring optionally contg. an addnl. heteroatom selected from O, S, NR3; D = -C0-6 alkylamino-C(:NR7)-NR15R16, -C0-6 alkylaminopyridyl, -C0-6 alkylaminoimidazolyl, -C0-6 alkylaminothiazolyl, -C0-6 alkylaminopyrimidinyl, -C0-6 alkylaminopiperazinyl-R15, -C0-6 alkylmorpholinyl, etc. (wherein R15, R16 = H, -C1-6 alkyl, -C0-3 alkylaryl, -C0-3 alkylheteroaryl, or -C0-3 alkyl-C3-8 cycloalkyl, wherein the alkyl and aryl groups are optionally substituted with one or two groups); X4 = H or C1-6 alkyl or X4 is taken together with R4 and the nitrogen atom to which X4 is attached and the carbon atom to which R4 is attached and form a five to seven membered ring] are prepd. Melanocortins are peptides derived from pro-opiomelanocortins (POMC) that bind to and activate G-protein coupled receptors (GPCR's) of the melanocortin receptor family and regulate a diverse no. of physiol. processes including food intake, metab., and thermogenesis as well as sexual dysfunction. These compds. I are useful for the treatment or prevention of disorders, diseases, or conditions responsive to the activation of melanocortin receptor including obesity, diabetes mellitus, male or female sexual dysfunction, erectile dysfunction, or disorders that cause redn. in appetite, or feeding behavior and/or body wt.; for modulating appetite and metabolic rates; for acutely stimulating the appetite for the treatment of hepatic lipidosis, cachexia, and other pathologies resulting in/from inappropriate food intake and wt. loss; for acutely stimulating the appetite of livestock for the treatment of ketosis, postpartum anestrus, and other metabolic and reproductive pathologies resulting in/from inappropriate food intake and wt. loss; and for enhancing growth and survivability of neonates in livestock. Thus, esterification of N-Boc-L-Tic-OH with N-hydroxysuccinimide using Et3N and EDC in CH2Cl2 at room temp. for 4 h gave 3,4-Dihydro-1H-isoquinoline-2,3-(S)-dicarboxylic acid 2-tert-Bu ester 3-(2,5-dioxopyrrolidin-1-yl) ester which was condensed with D-p-chlorophenylalanine in the presence of Et3N in CH2Cl2 at room temp. overnight to give 3-(S)-[(R)-1-Carboxy-2-(4-chlorophenyl)ethylcarbamoyl]-3,4-dihydro-1H-isoquinoline-2-carboxylic acid tert-Bu ester. The latter compd. was further condensed with 8a-(Pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)tetrahydroimidazo[1,5-a]pyrazine-1,3-dione using Et3N and EDC in CH2Cl2 at 0° for 5 h to give (S)-3-[(R)-1-(4-Chlorobenzyl)-2-[1,3-dioxo-8a-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)hexahydroimidazo[1,5-a]pyrazin-7-yl]-2-oxoethylcarbamoyl]-3,4-dihydro-1H-isoquinoline-2-carboxylic acid tert-Bu ester which was treated with a mixt. of EtOH and concd. HCl at 0° for 0.5 h to give (S)-1,2,3,4-Tetrahydroisoquinoline-3-carboxylic acid N-[(R)-1-(4-chlorobenzyl)-2-[1,3-dioxo-8a-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)hexahydroimidazo[1,5-a]pyrazin-7-yl]-2-oxoethyl]amide (II) hydrochloride which may be considered as a dipeptide analog hepterocycle amide, N-[N-(L-1,2,3,4-Tetrahydroisoquinoline-3-carbonyl)-D-p-chlorophenylalanyl]-1,3-dioxo-8a-(pyridin-2-ylmethyl)-2-(2,2,2-trifluoroethyl)hexahydroimidazo[1,5-a]pyrazine.

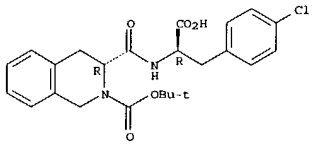
IT **252008-71-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of heterocycle compds. as melanocortin receptor ligands and therapeutic agents for treatment of prevention of obesity,

L4 ANSWER 84 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
diabetes mellitus, male or female sexual dysfunction)

RN 252008-71-2 CAPLUS

CN 2(1H)-Isoquinolinecarboxylic acid, 3-[[[(1R)-1-carboxy-2-(4-chlorophenyl)ethyl]amino]carbonyl]-3,4-dihydro-, 2-(1,1-dimethylethyl) ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



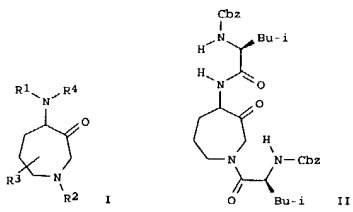
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 85 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:923616 CAPLUS
DOCUMENT NUMBER: 136:53691
TITLE: Preparation of 4-amino-azepan-3-one protease inhibitors
INVENTOR(S): Marquis, Robert W., Jr.; Ru, Yu; Veber, Daniel F.; Cummings, Maxwell D.; Thompson, Scott K.; Yamashita, Dennis
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 322 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001095911	A1	20011220	WO 2001-US19062	20010614
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1307204	A1	20030507	EP 2001-946344	20010614
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2004503502	T2	20040205	JP 2002-510089	20010614
BG 107327	A	20030731	BG 2002-107327	20021128
NO 2002005786	A	20030212	NO 2002-5786	20021202
PRIORITY APPLN. INFO.:			US 2000-593845 A2	20000614
			WO 2001-US19062 W	20010614

OTHER SOURCE(S): MARPAT 136:53691
GI



AB The title compds. [I; R1 = COCR13NR11R12, COCR13XR15, COCH2R13; R2 = H, alkyl, cycloalkylalkyl, etc.; R3 = H, alkyl, cycloalkylalkyl, etc.; R4 =

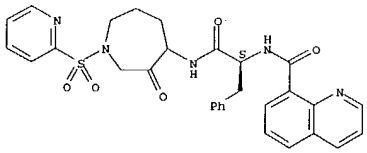
L4 ANSWER 85 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
H, alkyl, arylalkyl, etc.; R11 = H, alkyl, arylalkyl, etc.; R12 = H, alkyl, cycloalkyl, etc.; R13 = H, alkyl, alkenyl, etc.; R15 = H, alkyl, alkenyl, etc.] which inhibit proteases (no data), including cathepsin K, and are useful for treating diseases of excessive bone loss or cartilage or matrix degrdn. including osteoporosis, gingival disease including gingivitis and periodontitis, arthritis, more specifically, osteoarthritis and rheumatoid arthritis, Paget's disease, hypercalcemia of malignancy, and metabolic bone disease, were prepd. E.g., a multi-step synthesis of compd. II was given.

IT **281217-12-7P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-amino-azepan-3-one protease inhibitors)

RN 281217-12-7 CAPLUS

CN 8-Quinolinecarboxamide, N-[(1S)-2-[[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

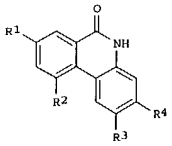


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 86 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:868423 CAPLUS
DOCUMENT NUMBER: 136:5923
TITLE: Preparation of sulfonamide/carbamide derivatives of 6(5H)phenanthridinones and their use as poly(ADP-ribose) polymerase (PARP) inhibitors
INVENTOR(S): Li, Jia-He; Kalish, Vincent J.; Zhang, Jie; Serdyuk, Larisa E.; Ferraris, Dana V.; Xiao, Ge; Kletzly, Paul W.
PATENT ASSIGNEE(S): Guilford Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001090077	A1	20011129	WO 2001-US15571	20010515
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002006927	A1	20020117	US 2001-854455	20010515

PRIORITY APPLN. INFO.: US 2000-205259P P 20000519
OTHER SOURCE(S): MARPAT 136:5923
GI



I

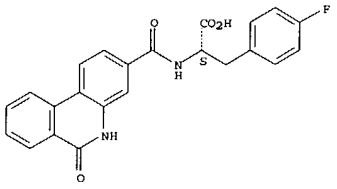
AB Title compds. I [R1 = H, halo; R2 = H, OH, NH2, NO, Me, aminomethyl, COOH; one of R3 and R4 = QP and the other of R3 and R4 is one of H, Me, CF3, NO2, amino, halo, piperazinyl, Q = A:O-X(Y), X(Y)-A:O; P = Z-amino, Z, (hetero)cycle; A = C, S:O; X = O, S, N, N-substituted amino acid provided that when X = O, S, Y = absent and when X = N, Y = H, alkyl, alkoxy, alkylamino, or Y, Z taken together to form a 5 - 7 membered heterocycle; Z = H, bond, C:O, (cyclo)alkyl, carboxy, etc.] were prepared Examples include

L4 ANSWER 86 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
19 synthetic examples, a PARP assay for 74 compds., models for focal cerebral ischemia, heart ischemia/reperfusion injury (rats) and gout. Examples also include an evaluation of neuroprotective effects on chronic constriction injury (rats). E.g., 2-amino-6(5H)phenanthridinone and 4-Me benzenesulfonyl chloride were reacted (dioxane, Et3N, 40°C, 30 h) to give I (R1, R2, R4 = H, R3 = NHSO2-C6H4-CH3-p; II) as a brown solid in 93% yield. II had IC50 = 0.12 μM for poly(ADP-ribose) polymerase (PARP). I are useful in the treatment of tissue damage resulting from cell damage due to apoptosis, neuronal mediated tissue damage, neurol. disorders, neurodegenerative diseases, etc.

IT **376609-03-9P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug; preparation of sulfonamide/carbamide derivs. of 6(5H)phenanthridinones and use as poly(ADP-ribose) polymerase (PARP) inhibitors)

RN 376609-03-9 CAPLUS
CN L-Phenylalanine, N-[(5,6-dihydro-6-oxo-3-phenanthridinyl)carbonyl]-4-fluoro- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 87 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:780691 CAPLUS
DOCUMENT NUMBER: 135:327371
TITLE: 4-Amino-azepan-3-one inhibitors of cathepsin L, their preparation, and their therapeutic use
INVENTOR(S): Cummings, Maxwell D.; Marquis, Robert W., Jr.; Ru, Yu; Thompson, Scott K.; Veber, Daniel F.; Yamashita, Dennis S.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001078734	A1	20011025	WO 2001-US12386	20010417
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1303281	A1	20030423	EP 2001-927076	20010417
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003531122	T2	20031021	JP 2001-576034	20010417
US 2004034013	A1	20040219	US 2002-258412	20021017

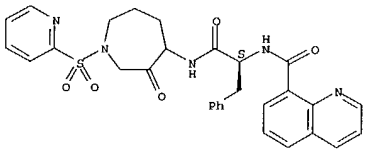
PRIORITY APPLN. INFO.: US 2000-197717P P 20000418
WO 2001-US12386 W 20010417
OTHER SOURCE(S): MARPAT 135:327371
AB Methods are provided which use 4-amino-azepan-3-one protease inhibitors of cathepsin L in the treatment of diseases in which cathepsin L is implicated, especially treatment or prevention of rheumatoid arthritis; cancer metastasis; diseases requiring inhibition of tissue destruction by macrophages, particularly lung macrophages, such as asthma, chronic obstructive pulmonary disease (COPD), and emphysema; and diseases requiring, for therapy, inhibition of pos. selection of CD4+T- cells by cortical thymic epithelial cells.

IT **281217-12-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(aminoazepanone inhibitors of cathepsin L, preparation, and therapeutic use)

RN 281217-12-7 CAPLUS
CN 8-Quinolinecarboxamide, N-[(1S)-2-[[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 87 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 88 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:764908 CAPLUS
DOCUMENT NUMBER: 136:65517
TITLE: The pH-Dependent Primary Photoreactions of Ochratoxin A
AUTHOR(S): Il'ichev, Yuri V.; Perry, Jennifer L.; Manderville, Richard A.; Chignell, Colin F.; Simon, John D.
CORPORATE SOURCE: Department of Chemistry, Duke University, Durham, NC, 27708, USA
SOURCE: Journal of Physical Chemistry B (2001), 105(45), 11369-11376
CODEN: JPCBFK; ISSN: 1089-5647
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

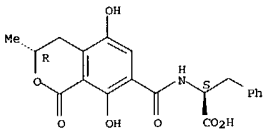
AB Steady-state and time-resolved spectroscopies are used to elucidate the primary photoprocesses following the excitation of ochratoxin A (OTA), its dechlorinated derivative ochratoxin B (OTB), and O-Me ether of OTA (MOA). The excited-state dynamics of OTA and OTB depend on the protonation of the isocoumarin moiety. Fluorescence spectra of the protonated forms reveal anomalously large Stokes shifts that are attributed to the enol tautomer formed via an intramol. excited-state proton transfer. No evidence for "normal" emission of the keto form of OTA and OTB is found even in aqueous solns. MOA, which lacks a proton on the phenol moiety and exists, therefore, only in the keto form, exhibits weak fluorescence with a substantially smaller Stokes shift. The deprotonated species show relatively strong emission typical for phenolate anions. OTA decomps. slowly upon UV irradiation in aqueous solns. The photoreaction quantum yield varies significantly with solution pH and O2 concentration The highest yield is observed for the deprotonated form of OTA in deoxygenated solns. The corresponding hydroquinone (OHQ) is identified as a major photoproduct. Monophotonic photoionization of the fully deprotonated OTA in aqueous solution is demonstrated with nanosecond laser flash photolysis. In the absence of O2 and other scavengers, hydrated electrons are trapped by OTA in the ground state with the diffusion-controlled rate constant Photoirradn. of OTA in the presence of supercoiled plasmid DNA results in the formation of relaxed circular DNA. The yield of circular DNA correlates with the quantum yield of OTA photodecompositon in these solns., because the photocleavage efficiency is higher in the absence of O2 and at basic pH.

IT **205034-32-8**
RL: CPS (Chemical process); FMU (Formation, unclassified); PEP (Physical, engineering or chemical process); PRP (Properties); FORM (Formation, nonpreparative); PROC (Process)
(pH-dependent primary photoreactions of ochratoxin A)

RN 205034-32-8 CAPLUS
CN L-Phenylalanine, N-[[(3R)-3,4-dihydro-5,8-dihydroxy-3-methyl-1-oxo-1H-2-benzopyran-7-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

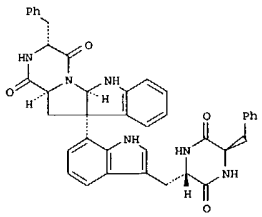
L4 ANSWER 88 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 105 THERE ARE 105 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 89 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:636473 CAPLUS
DOCUMENT NUMBER: 135:344629
TITLE: Total Synthesis of Asperazine
AUTHOR(S): Govek, Steven P.; Overman, Larry E.
CORPORATE SOURCE: Department of Chemistry, University of California, Irvine, CA, 92697-2025, USA
SOURCE: Journal of the American Chemical Society (2001), 123(38), 9468-9469
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

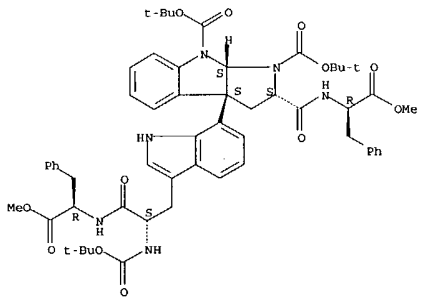
AB The first total synthesis of asperazine (I) was accomplished in 22 steps from readily avaliable starting materials. This synthesis confirms the structure of asperazine and provides yet another example of the tremendous utility of intramol. Heck reactions for forging highly congested quaternary carbon centers.

IT **370890-28-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(total synthesis of asperazine)

RN 370890-28-1 CAPLUS
CN D-Phenylalanine, 7-[(2S,3aS,8aS)-1,8-bis[(1,1-dimethylethoxy)carbonyl]-2,3,8,8a-tetrahydro-2-[[[(1R)-2-methoxy-2-oxo-1-(phenylmethyl)ethyl]amino]carbonyl]pyrrolo[2,3-b]indol-3a(1H)-yl]-N-[(1,1-dimethylethoxy)carbonyl]-L-tryptophyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 89 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

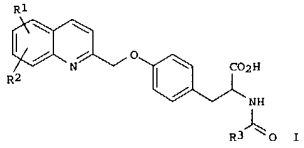


REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 90 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:597979 CAPLUS
DOCUMENT NUMBER: 135:167035
TITLE: Preparation of tyrosine derivatives having anti-leukotriene activity
INVENTOR(S): Makovec, Francesco; Peris, Walter; Rovati, Lucio Claudio
PATENT ASSIGNEE(S): Rotta Research Laboratorium S.P.A., Italy
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

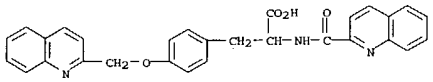
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001058892	A1	20010816	WO 2001-EP1315	20010207
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
IT 1320162	B1	20031118	IT 2000-TO127	20000209
EP 1255749	A1	20021113	EP 2001-905744	20010207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003522768	T2	20030729	JP 2001-558442	20010207
US 2003087910	A1	20030508	US 2002-203424	20020808
US 6605722	B2	20030812		

PRIORITY APPLN. INFO.: IT 2000-TO127 A 20000209
WO 2001-EP1315 W 20010207
OTHER SOURCE(S): MARPAT 135:167035
GI



AB Compds. I [R1, R2 = H, C1-4 alkyl, halo, MeO, cyano, CF3; R3 = (un)substituted Ph, pyridyl or (iso)quinolinyl, 1- or 2-naphthyl, 2- or 3-indolyl or N-alkyl derivs., 2-, 5- or 6-quinoxalyl, cinnolyl, benzimidazolyl], which may have the L- or D-configuration or be racemic, were prepared and are useful in the treatment of pathol. conditions sensitive to leukotriene inhibition. Thus, O-(2-quinolinylmethyl)-N-quinaldoyl-DL-tyrosine was prepared by acylation of DL-tyrosine Me ester with quinaldic acid, O-alkylation with 2-chloromethylquinoline hydrochloride, and saponification The product showed IC50x10-9 M = 20.0 for inhibition of binding of [3H]-LTD4 to guinea pig lung membranes.

L4 ANSWER 90 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
IT **353798-73-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tyrosine derivs. having anti-leukotriene activity)
RN 353798-73-9 CAPLUS
CN Tyrosine, N-(2-quinolinylcarbonyl)-O-(2-quinolinylmethyl)- (9CI) (CA INDEX NAME)

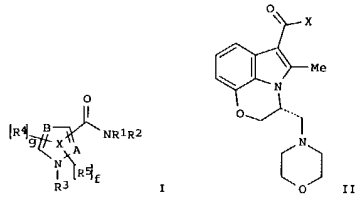


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 91 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:597958 CAPLUS
DOCUMENT NUMBER: 135:166827
TITLE: Preparation of 1H-indole-3-carboxamides, 1H-indazole-3-carboxamides, 1H-pyrido[4,3-b]indol-1-ones and pyrrolo[1,2,3-de]-1,4-benzoxazine-6-carboxamides as cannabinoid receptor modulators for treating respiratory and non-respiratory diseases
INVENTOR(S): Leftheris, Katerina; Zhao, Rulin; Chen, Bang-Chi; Kiener, Peter; Wu, Hong; Pandit, Chennagiri R.; Wrobleski, Stephen; Chen, Ping; Hynes, John, Jr.; Longphre, Malinda; Norris, Derek J.; Spergel, Steven; Tokarski, John
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA; et al.
SOURCE: PCT Int. Appl., 199 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001058869	A2	20010816	WO 2001-US4131	20010208
WO 2001058869	A3	20020124		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1254115	A2	20021106	EP 2001-907144	20010208
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004502642	T2	20040129	JP 2001-558420	20010208

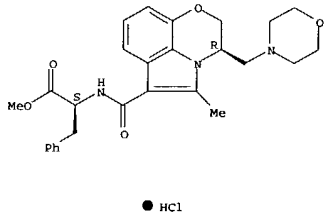
PRIORITY APPLN. INFO.: US 2000-181818P P 20000211
WO 2001-US4131 W 20010208
OTHER SOURCE(S): MARPAT 135:166827
GI



L4 ANSWER 91 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

AB The title compds. [I; A, B = C, N so that ring X = pyrrole, pyrazole or imidazole (wherein when A = N, the group CONR1R2 is attached to atom C-3 and R5 does not exist; and when A = C, one of CONR1R2 and R5 is attached to A and the other to atom C-3; and when B = C, two R4 groups attached to B and atom C-5, resp., form a fused 6-membered hetroaryl); f = 0-1; g = 1-2; R1, R2 = H, alkyl, heterocycloalkyl, etc.; R2 together with R1 or R5 forms a 5-6 membered heterocyclo; R3 = H, alkyl, aryl, etc.; R4 is attached to atom C-5 and optionally B and is H, alkyl, aryl, etc.; R5 is attached to A or atom C-3 and is H, alkyl, aryl, etc.; R5 together with R2 forms a heterocyclo], useful as cannabinoid receptor modulators (no data given) for treating respiratory and non-respiratory leukocyte-activation associated diseases, were prepared Thus, reacting the acid chloride II [X = Cl] (multi-step synthesis given) with 2,2,6,6-tetramethylcyclohexylamine afforded the pyrrolo[1,2,3-de]-1,4-benzoxazine-6-carboxamide II [X = 2,2,6,6-tetramethylcyclohexylamino].
IT **354569-38-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 1H-indole-3-carboxamides, 1H-indazole-3-carboxamides, 1H-pyrido[4,3-b]indol-1-ones and pyrrolo[1,2,3-de]-1,4-benzoxazine-6-carboxamides as cannabinoid receptor modulators for treating respiratory and non-respiratory diseases)
RN 354569-38-3 CAPLUS
CN L-Phenylalanine, N-[[(3R)-2,3-dihydro-5-methyl-3-(4-morpholinylmethyl)pyrrolo[1,2,3-de]-1,4-benzoxazin-6-yl]carbonyl]-, methyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



● HCl

L4 ANSWER 92 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

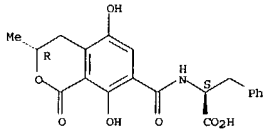
ACCESSION NUMBER: 2001:594827 CAPLUS
DOCUMENT NUMBER: 135:314766
TITLE: Electrochemical Oxidation of Ochratoxin A: Correlation with 4-Chlorophenol
AUTHOR(S): Calcutt, M. Wade; Gillman, Ivan G.; Noftle, Ronald E.; Manderville, Richard A.
CORPORATE SOURCE: Department of Chemistry, Wake Forest University, Winston-Salem, NC, 27109-7486, USA
SOURCE: Chemical Research in Toxicology (2001), 14(9), 1266-1272
CODEN: CRTOEC; ISSN: 0893-228X
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ochratoxin A (OTA) is a mycotoxin implicated in human kidney carcinogenesis, in which oxidative activation is believed to play a key role. To gain an understanding of the oxidative behavior of the toxin, we have carried out an electrochem. study and have observed a direct correlation between the electrochem. of OTA and 4-chlorophenol (4-ClPhOH). Cyclic voltammetry (CV) of OTA in acetonitrile (MeCN) showed that the toxin exhibits an irreversible oxidative half-peak potential (Ep/2) of 1.81 V vs. SCE ; the corresponding value for 4-ClPhOH is 1.59 V. For both compds., subsequent scans revealed the appearance of the resp. hydroquinone/benzoquinone couple, which formed from the oxidation of the parent para-chlorophenol moiety. The hydroquinone of OTA (OTHQ) exhibited Ep/2 = 1.21 V in MeCN. Deprotonation of OTA to form the phenolate (OTA-) lowered the potential to Ep/2 = 1.0 V in MeCN. However, from the oxidation of OTA, no evidence for the OTHQ/OTQ redox couple was found. In aqueous phosphate buffer (pH 6-8), the electrochem. behavior of OTA mimicked that observed for OTA- in MeCN; Ep/2 was .apprx.0.8 V vs. SCE and subsequent scans did not generate the OTHQ/OTQ redox couple. From capillary electrophoresis (CE), a diffusion coefficient (D) of 0.48+10-5 cm2 s-1 was determined for OTA in phosphate buffer, pH 7.0. Combining this value with electrochem. data suggested that OTA undergoes a 1H+/1e oxidation in aqueous media. The biol. implications of these findings with respect to the oxidative metabolism of OTA, and other chlorinated phenols, are discussed.

IT **205034-32-8**
RL: FMU (Formation, unclassified); PRP (Properties); FORM (Formation, nonpreparative)
(electrochem. oxidation of ochratoxin A and correlation with chlorophenol)

RN 205034-32-8 CAPLUS
CN L-Phenylalanine, N-[[(3R)-3,4-dihydro-5,8-dihydroxy-3-methyl-1-oxo-1H-2-benzopyran-7-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 92 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 93 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

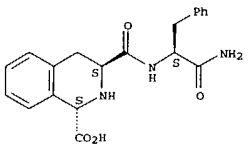
ACCESSION NUMBER: 2001:584421 CAPLUS
DOCUMENT NUMBER: 135:318403
TITLE: Asymmetric Pictet-Spengler reactions: synthesis of 1,2,3,4-tetrahydroisoquinoline carboxylic acid (Tic) chimeras
AUTHOR(S): Spengler, Jan; Schedel, Hartmut; Sieler, Joachim; Quaedflieg, Peter J. L. M.; Broxterman, Quirinus B.; Duchateau, Alexander L. L.; Burger, Klaus
CORPORATE SOURCE: Department of Organic Chemistry, University of Leipzig, Leipzig, 04103, Germany
SOURCE: Synthesis (2001), (10), 1513-1518
CODEN: SYNTBF; ISSN: 0039-7881
PUBLISHER: Georg Thieme Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:318403

AB A preparatively simple diastereoselective synthesis of the amino acid chimera (1S,3S)-1,2,3,4-tetrahydroisoquinoline-1,3-dicarboxylic acid from hexafluoroacetone-protected phenylalanine and glyoxylic acid hydrate via Pictet-Spengler reaction is described. The potential of the reaction of hexafluoroacetone-protected phenylalanine with other aldehydes was scrutinized.

IT **367952-41-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

RN 367952-41-8 CAPLUS
CN 1-Isoquinolinecarboxylic acid, 3-[[[(1S)-2-amino-2-oxo-1-(phenylmethyl)ethyl]amino]carbonyl]-1,2,3,4-tetrahydro-, (1S,3S)- (9CI) (CA INDEX NAME)

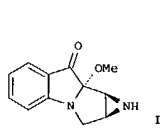
Absolute stereochemistry. Rotation (-).



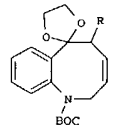
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 94 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

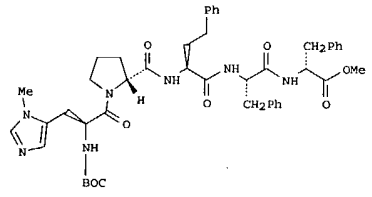
ACCESSION NUMBER: 2001:558409 CAPLUS
DOCUMENT NUMBER: 135:288611
TITLE: Enantioselective Synthesis of a Mitosane Core Assisted by Diversity-Based Catalyst Discovery
AUTHOR(S): Papaioannou, Nikolaos; Evans, Catherine A.; Blank, Jarred T.; Miller, Scott J.
CORPORATE SOURCE: Department of Chemistry Merkert Chemistry Center, Boston College, Chestnut Hill, MA, 02467-3860, USA
SOURCE: Organic Letters (2001), 3(18), 2879-2882
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:288611
GI



I



II



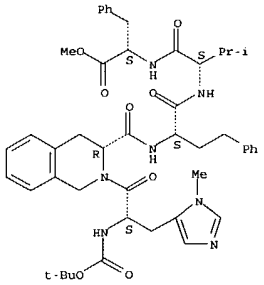
III

AB Synthesis of (-)-mitosane I in optically pure form is reported. A retrosynthetic plan that proceeds through racemic allylic alc. II (R = OH) was carried out. Intermediate II served as a test substrate for a rapid screen of a small library (152 members) of peptide-based kinetic resolution catalysts. Peptide III was found to effect kinetic resolution with krel = 27. Alc. II (R = β-OH) was then converted to optically pure I in eight steps.

IT **365223-05-8P**
RL: CAT (Catalyst use); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation); USES (Uses)
(enantioselective synthesis of a mitosane core assisted by diversity-based catalyst discovery)

L4 ANSWER 94 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 365223-05-8 CAPLUS
CN L-Phenylalanine, N-[(1,1-dimethylethoxy)carbonyl]-3-methyl-L-histidyl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(αS)-α-aminobenzenebutanoyl-L-valyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

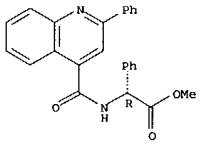


REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 95 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:527755 CAPLUS
DOCUMENT NUMBER: 135:266637
TITLE: Is There a Difference between Leads and Drugs? A Historical Perspective
AUTHOR(S): Oprea, Tudor I.; Davis, Andrew M.; Teague, Simon J.; Leeson, Paul D.
CORPORATE SOURCE: AstraZeneca R&D Molndal EST Lead Informatics, Moelndal, S 431 83, Swed.
SOURCE: Journal of Chemical Information and Computer Sciences (2001), 41(5), 1308-1315
CODEN: JCISD8; ISSN: 0095-2338
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To be considered for further development, lead structures should display the following properties: (1) simple chemical features, amenable for chemical optimization; (2) membership to an established SAR series; (3) favorable patent situation; and (4) good absorption, distribution, metabolism, and excretion (ADME) properties. There are two distinct categories of leads: those that lack any therapeutic use (i.e., "pure" leads), and those that are marketed drugs themselves but have been altered to yield novel drugs. We have previously analyzed the design of leadlike combinatorial libraries starting from 18 lead and drug pairs of structures (S. J. Teague et al. Angew. Chemical, Int. Ed. Engl. 1999, 38, 3743-3748). Here, we report results based on an extended dataset of 96 lead-drug pairs, of which 62 are lead structures that are not marketed as drugs, and 75 are drugs that are not presumably used as leads. We examined the following properties: MW (mol. weight), CMR (the calculated mol. refractivity), RNG (the number of rings), RTB (the number of rotatable bonds), the number of hydrogen bond donors (HDO) and acceptors (HAC), the calculated logarithm of the n-octanol/water partition (CLogP), the calculated logarithm of the distribution coefficient at pH 7.4 (LogD74), the Daylight-fingerprint druglike score (DFPS), and the property and pharmacophore features score (PPFS). The following differences were observed between the medians of drugs and leads: ΔMW = 69; ΔCMR = 1.8; ΔRNG = ΔHAC =1; ΔRTB = 2; ΔCLogP = 0.43; ΔLogD74 = 0.97; ΔHDO = 0; ΔDFPS = 0.15; ΔPPFS = 0.12. Lead structures exhibit, on the average, less mol. complexity (less MW, less number of rings and rotatable bonds), are less hydrophobic (lower CLogP and LogD74), and less druglike (lower druglike scores). These findings indicate that the process of optimizing a lead into a drug results in more complex structures. This information should be used in the design of novel combinatorial libraries that are aimed at lead discovery.
IT **174635-53-1**, SB 218795 R
RL: PRP (Properties)
(drug design and structure-activity relationship between leads and leadlike drugs)
RN 174635-53-1 CAPLUS
CN Benzeneacetic acid, α-[[(2-phenyl-4-quinolinyl)carbonyl]amino]-, methyl ester, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

L4 ANSWER 95 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



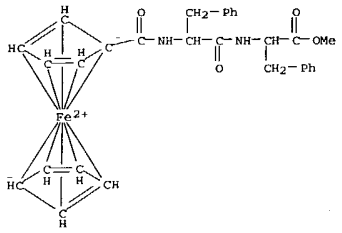
REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 96 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:514247 CAPLUS
DOCUMENT NUMBER: 135:257449
TITLE: Interaction of Ferrocenoyl-Dipeptides with 3-Aminopyrazole Derivatives: β-Sheet Models? A Synthetic, Spectroscopic, Structural, and Electrochemical Study
AUTHOR(S): Saweczko, Pete; Enright, Gary D.; Kraatz, Heinz-Bernhard
CORPORATE SOURCE: Department of Chemistry, University of Saskatchewan, Saskatoon, SK, S7N 5C9, Can.
SOURCE: Inorganic Chemistry (2001), 40(17), 4409-4419
CODEN: INOCAJ; ISSN: 0020-1669
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:257449
AB The use of 3-aminopyrazole deriva. as β-sheet templates is investigated using a series of ferrocenoyl-dipeptides [Fc-(Gly)2-OEt, Fc-(Ala)2-OCH2Ph, Fc-Leu-Phe-OMe, Fc-Val-Phe-OMe, Fc-(Phe)2-OMe, Fc-(Leu)2-OMe, Fc-(Val)2-OMe]. The synthesis and full characterization of the ferrocenoyl-dipeptides are reported. The solid-state structures of Fc-(Gly)2-OMe and Fc-Leu-Phe-OMe show extensive hydrogen bonding of the podand peptide substituents, resulting in the formation of supramol. Fc-dipeptide assemblies. For Fc-(Gly)2-OMe, this can be described as a parallel β-sheet, whereas intermol. interactions in Fc-Leu-Phe-OMe result in the formation of supramol. helical structures. The saturation titrns. of Fc-dipeptides with 3-amino-5-methylpyrazole (3-AMP) and 3-trifluoroacetamido-5-methylpyrazole (3-TFAc-AMP) show a 1:1 interaction of the Fc-peptide with the aminopyrazole deriva. IR measurements in solution confirm binding to the top face of the Fc-dipeptide and the involvement of the Fc-C:O and the ester C:O groups in establishing H-bonding interactions with the 3-TFAc-AMP. However, binding consts. in chloroform are low and range from 8 to 27 M-1, which correspond to binding energies of 5-7 kJ mol-1. In higher polarity solvents, such as acetonitrile or acetone, the binding consts. are below 5 M-1, emphasizing the limited utility of 3-AMP deriva. as β-sheet templates. Electrochem. measurements confirm the weak interactions between the various Fc-dipeptides and 3-TFAc-AMP. Typical shifts in the redox potential of the Fc moiety are in the range 0-20 mV. Attempts to modify 3-AMP at the 3-position by carbodiimide coupling with Boc-Aib-OH (in order to enhance the binding to the Fc-peptides) resulted in 2-(Boc-Aib)-substituted 3-AMP deriva. Substitution at the 2-position blocks the binding site, and no interactions with Fc-dipeptides are observed
IT **362056-37-9**
RL: FMU (Formation, unclassified); PRP (Properties); FORM (Formation, nonpreparative)
(association consts. for the 1:1 interaction complexes of (ferrocenoyl)dipeptides with aminopyrazoles as β-sheet templates)
RN 362056-37-9 CAPLUS
CN L-Phenylalanine, N-(ferrocenylcarbonyl)-L-phenylalanyl-, methyl ester, compd. with 5-methyl-1H-pyrazol-3-amine (1:1) (9CI) (CA INDEX NAME)

CM 1

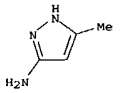
CRN 245123-57-3
CMF C30 H30 Fe N2 O4
CCI CCS

L4 ANSWER 96 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



CM 2

CRN 31230-17-8
CMF C4 H7 N3



REFERENCE COUNT: 70 THERE ARE 70 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 97 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:436800 CAPLUS
DOCUMENT NUMBER: 135:178024
TITLE: Novel sesquiterpenoids from the roots of Phyllanthus emblica
AUTHOR(S): Zhang, Ying-Jun; Tanaka, Takashi; Iwamoto, Yoko; Yang, Chong-Ren; Kouno, Isao
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Nagasaki University, Nagasaki, 852-8521, Japan
SOURCE: Journal of Natural Products (2001), 64(7), 870-873
CODEN: JNPRDF; ISSN: 0163-3864
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

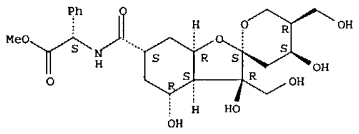
AB Three novel bisabolane-type sesquiterpenoids, phyllaemblic acids B (I) and C (II) and phyllaemblicin D (III), together with two new phenolic glycosides, 2-carboxylmethylphenol 1-O-β-D-glucopyranoside (IV) and 2,6-dimethoxy-4-(2-hydroxyethyl)phenol 1-O-β-D-glucopyranoside (V), were isolated from the roots of Phyllanthus emblica. The structures of I-V were established by spectral and chemical methods. The absolute stereochem.
of I and II was determined by applying the PGME method.

IT **354813-54-0P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and properties of)

RN 354813-54-0 CAPLUS

CN Benzeneacetic acid, α-[[[(2'S,3R,3aS,4R,4'S,5'R,6S,7aR)-3',3a,4,4',5,5',6,6',7,7a-decahydro-3,4,4'-trihydroxy-3,5'-bis(hydroxymethyl)spiro[benzofuran-2(3H),2'-[2H]pyran]-6-yl]carbonyl]amino]-, methyl ester, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



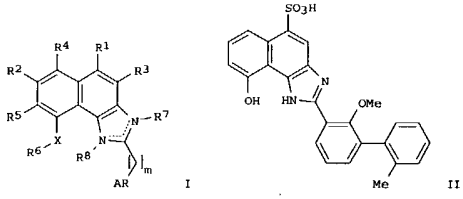
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 98 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:416769 CAPLUS
DOCUMENT NUMBER: 135:33476
TITLE: Preparation of naphth[1,2-d]imidazoles as thrombopoietin mimetics
INVENTOR(S): Luengo, Juan I.; Duffy, Kevin J.; Price, Alan T.; Zhang, Lihua
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 90 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001039773	A1	20010607	WO 2000-US33432	20001206
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
EP 1244446	A1	20021002	EP 2000-984123	20001206
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR				
JP 2003515560	T2	20030507	JP 2001-541505	20001206
US 2003083361	A1	20030501	US 2002-148945	20020912

PRIORITY APPLN. INFO.: US 1999-169130P P 19991206
WO 2000-US33432 W 20001206
OTHER SOURCE(S): MARPAT 135:33476
GI



I

II

AB The title compds. [I; R1-R5 = H, CO2R11, alkyl, etc. (wherein R11 = H, alkyl, cycloalkyl, etc.); R6 = H, alkyl, cycloalkyl, etc.; R7, R8 = absent, H, alkyl, etc.; m = 0-6; X = S, O, NH, etc.; AR = (un)substituted cyclic or polycyclic aromatic ring containing from 3-16 carbon atoms, optionally
containing one or more heteroatoms] and their pharmaceutically acceptable salts which are non-peptide TPO mimetics, and are useful in enhancing platelet production, were prepared and formulated. E.g., a 3-step synthesis of the title compound II.HCl was described. Biol. data for compds. I were given.

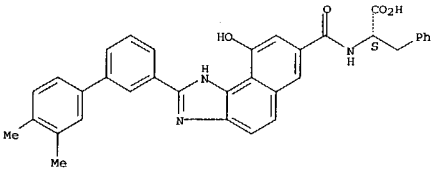
L4 ANSWER 98 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

IT **343603-01-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of naphth[1,2-d]imidazoles as thrombopoietin mimetics)

RN 343603-01-0 CAPLUS

CN L-Phenylalanine, N-[[2-(3',4'-dimethyl[1,1'-biphenyl]-3-yl)-9-hydroxy-1H-naphth[1,2-d]imidazol-7-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

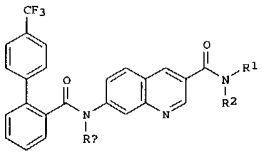


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 99 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:356253 CAPLUS
DOCUMENT NUMBER: 134:366810
TITLE: Preparation of 7-[(4'-trifluoromethyl-biphenyl-2-carbonyl)amino]-quinoline-3-carboxylic acid amides for inhibiting the secretion of apolipoprotein B
INVENTOR(S): Bertinato, Peter; Hamanaka, Ernest Seiichi; Ruggeri, Roger Benjamin; Wilson, Douglas Paul
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 124 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1099701	A1	20010516	EP 2000-309947	20001109
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000005322	A	20010717	BR 2000-5322	20001109
US 6369075	B1	20020409	US 2000-711281	20001109
JP 2001139555	A2	20010522	JP 2000-344267	20001110
US 2002132806	A1	20020919	US 2002-54455	20020122
US 6713489	B2	20040330		

PRIORITY APPLN. INFO.: US 1999-164803P P 19991110
US 2000-224956P P 20000811
US 2000-711281 A3 20001109
OTHER SOURCE(S): MARPAT 134:366810
GI

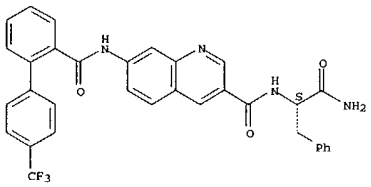


I

AB The title compds. [I; R1 = H, alkyl; R2 = H, alkyl, CHX2, etc.; NR1R2 = 3-7 membered heterocycloalkyl comprising 1-3 heteroatoms; X = (un)substituted aryl, heteroaryl, etc.; Rb = H, alkyl] that inhibit the secretion of apolipoprotein B and/or inhibit microsomal triglyceride transfer protein, and therefore useful in treating and/or preventing atherosclerosis, obesity, diabetes, hyperlipidemia, hyperlipoproteinemia, hypercholesterolemia, hypertriglyceridemia, hypoalphalipoproteinemia, pancreatitis, myocardial infarction, stroke, restenosis, or Syndrome X,

L4 ANSWER 99 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
were prepd. E.g., a multi-step synthesis of I [R1 = H; R2 = CH(2-pyridyl)2] was given.
IT **339290-34-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 7-[(4'-trifluoromethyl-biphenyl-2-carbonyl)amino]-quinoline-3-carboxylic acid amides for inhibiting the secretion of apolipoprotein B)
RN 339290-34-5 CAPLUS
CN 3-Quinolinecarboxamide, N-[(1S)-2-amino-2-oxo-1-(phenylmethyl)ethyl]-7-[[[4'-(trifluoromethyl)[1,1'-biphenyl]-2-yl]carbonyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



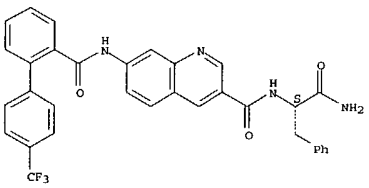
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 100 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:356207 CAPLUS
DOCUMENT NUMBER: 134:348283
TITLE: Methods of administering apolipoprotein B secretion/microsomal triglyceride transfer protein inhibitors
INVENTOR(S): Chang, George; Vincent, John
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 42 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1099442	A2	20010516	EP 2000-309907	20001108
EP 1099442	A3	20021204		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: US 1999-164579P P 19991110
OTHER SOURCE(S): MARPAT 134:348283
AB Methods are provided for administration of apoB secretion/MTP inhibitors. The methods comprise administration prior to or during a period of somnolence. Preparation of inhibitors is also described.
IT **339290-34-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(apolipoprotein B secretion/microsomal triglyceride transfer protein inhibitor administration prior to or during somnolence period)
RN 339290-34-5 CAPLUS
CN 3-Quinolinecarboxamide, N-[(1S)-2-amino-2-oxo-1-(phenylmethyl)ethyl]-7-[[[4'-(trifluoromethyl)[1,1'-biphenyl]-2-yl]carbonyl]amino]- (9CI) (CA INDEX NAME)

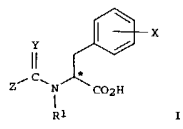
Absolute stereochemistry.



L4 ANSWER 101 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:338483 CAPLUS
DOCUMENT NUMBER: 134:353176
TITLE: Preparation of urea derivatives as VLA-4 antagonists
INVENTOR(S): Okuyama, Akihiko; Ikegami, Satoru; Harada, Tatsuhiro; Maruyama, Tatsuya; Matsumura, Yuzuru; Nagata, Naoya; Fukui, Hideto; Fujimoto, Kyouko
PATENT ASSIGNEE(S): Kaken Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 72 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032610	A1	20010510	WO 2000-JP7571	20001027
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: JP 1999-310316 A 19991029
OTHER SOURCE(S): MARPAT 134:353176
GI

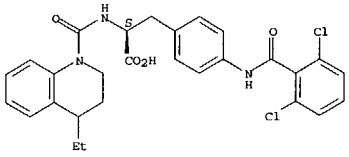


I

AB The title compds. I [R1 is hydrogen, alkyl, etc.; X is hydrogen, halogeno, alkyl, aryl, arylamide, etc.; Y is oxygen or sulfur; and Z is a hydrocarbon or heterocyclic group containing a nitrogen atom through which Z is bonded to the carbon atom of CY; the asterisk indicates an asym. carbon] are prepared. Processes for the preparation of I are also claimed. Several compds. of this invention in vitro at 0.01 nM to 3.7 nM gave 50% inhibition of VLA-4/VCAM-1 adhesion.
IT **339001-71-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of urea derivs. as VLA-4 antagonists)
RN 339001-71-7 CAPLUS
CN L-Phenylalanine, 4-[(2,6-dichlorobenzoyl)amino]-N-[(4-ethyl-3,4-dihydro-1(2H)-quinolinyl)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 101 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 102 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

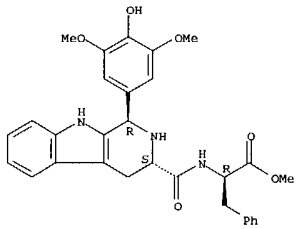
ACCESSION NUMBER: 2001:330818 CAPLUS
DOCUMENT NUMBER: 135:137682
TITLE: The synthesis of amino acid-functionalized β-carbolines as topoisomerase II inhibitors
AUTHOR(S): Deveau, A. M.; Labroli, M. A.; Dieckhaus, C. M.; Barthen, M. T.; Smith, K. S.; Macdonald, T. L.
CORPORATE SOURCE: Department of Chemistry, University of Virginia, Charlottesville, VA, 22901, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(10), 1251-1255
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:137682

AB The synthesis and biol. activity of amino acid-functionalized β-carboline derivs., which are structurally related to azatoxin and the tryprostatins, are reported. These compds. were assayed for their growth inhibition properties in H520 and PC3 cell lines and were examined for their abilities to inhibit topoisomerase II-mediated DNA relaxation.

IT **352015-64-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis of amino acid-functionalized β-carbolines as topoisomerase II inhibitors)

RN 352015-64-6 CAPLUS
CN D-Phenylalanine, N-[[(1R,3S)-2,3,4,9-tetrahydro-1-(4-hydroxy-3,5-dimethoxyphenyl)-1H-pyrido[3,4-b]indol-3-yl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 103 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

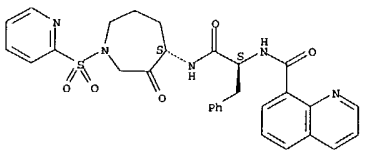
ACCESSION NUMBER: 2001:318582 CAPLUS
DOCUMENT NUMBER: 135:120165
TITLE: Potent and selective cathepsin L inhibitors do not inhibit human osteoclast resorption in vitro
AUTHOR(S): James, Ian E.; Marquis, Robert W.; Blake, Simon M.; Hwang, Shing Mei; Gress, Catherine J.; Ru, Yu; Zembryki, Denise; Yamashita, Dennis S.; McQueney, Michael S.; Tomaszek, Thaddeus A.; Oh, Hye-Ja; Gowen, Maxine; Veber, Daniel F.; Lark, Michael W.
CORPORATE SOURCE: Departments of Bone and Cartilage Biology, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406, USA
SOURCE: Journal of Biological Chemistry (2001), 276(15), 11507-11511
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cathepsins K and L are related cysteine proteases that have been proposed to play important roles in osteoclast-mediated bone resorption. To further examine the putative role of cathepsin L in bone resorption, we have evaluated selective and potent inhibitors of human cathepsin L and cathepsin K in an in vitro assay of human osteoclastic resorption and an in situ assay of osteoclast cathepsin activity. The potent selective cathepsin L inhibitors (Ki = 0.0099, 0.034, and 0.27 nM) were inactive in both the in situ cytochem. assay (IC50 > 1 μM) and the osteoclast-mediated bone resorption assay (IC50 > 300 nM). Conversely, the cathepsin K selective inhibitor was potently active in both the cytochem. (IC50 = 63 nM) and resorption (IC50 = 71 nM) assays. A recently reported dipeptide aldehyde with activity against cathepsins L (Ki = 0.052 nM) and K (Ki = 1.57 nM) was also active in both assays (IC50 = 110 and 115 nM, resp.) These data confirm that cathepsin K and not cathepsin L is the major protease responsible for human osteoclastic bone resorption.

IT **350796-41-7**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(potent and selective cathepsin L inhibitors do not inhibit human osteoclast resorption in vitro)

RN 350796-41-7 CAPLUS
CN 8-Quinolinecarboxamide, N-[(1S)-2-[[(4S)-hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-2-oxo-1-(phenylmethyl)ethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 103 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

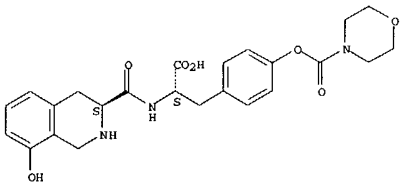
L4 ANSWER 104 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:228855 CAPLUS
DOCUMENT NUMBER: 134:252658
TITLE: Preparation of tyrosine derivatives as inhibitors of α4 containing integrin-mediated binding to ligands VCAM-1 and MAdCAM.
INVENTOR(S): Jackson, David Y.; Sailes, Frederick C.; Sutherlin, Daniel P.
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 86 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001021584	A1	20010329	WO 2000-US26326	20000925
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1214292	A1	20020619	EP 2000-965417	20000925
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
US 6469047	B1	20021022	US 2000-669779	20000925
JP 2003509488	T2	20030311	JP 2001-524964	20000925

PRIORITY APPLN. INFO.: US 1999-156062P P 19990924
WO 2000-US26326 W 20000925
OTHER SOURCE(S): MARPAT 134:252658
AB Tyrosine derivs., e.g., ArCH2CH[N(A)(Z)]CO-Y [Z = H, alkyl; A = B(CH2)q-X-, where B = (un)substituted Ph and X = CO, SO2, null or B = cyanoalkyl, carbocyclyl or heterocyclyl and X = CO; R6 = H, alkyl, amino, cyano, hydroxy, alkylsulfonyl, etc.; q = 0-3; Y is H, (un)substituted alkoxy, alkoxyalkoxy, aryloxy, alkylaminoalkoxy, dialkylaminoalkoxy,alkylamino, arylamino, heterocyclyl or heteroarylalkyl; Ar is Ph which has hydroxy, carbonate, thiocarbonate, carbamoyloxy or acyloxy groups and optionally other substituents] were prepared as inhibitors of α4 containing integrin-mediated binding to ligands such as VCAM-1 and MAdCAM. Methods of synthesis are described and inhibitory binding data are tabulated for 416 compds., including N-(o-chlorobenzoyl)-O-(allylcarbamoyl)-L-tyrosine, for which IC50 is < 1.0 micromolar.
IT **331470-84-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tyrosine derivs. as inhibitors of α4 containing integrin-mediated binding to ligands VCAM-1 and MAdCAM.)
RN 331470-84-9 CAPLUS
CN L-Tyrosine, N-[[(3S)-1,2,3,4-tetrahydro-8-hydroxy-3-isoquinolinyl]carbonyl]-, 4-(4-morpholinecarboxylate) (9CI) (CA INDEX NAME)

L4 ANSWER 104 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

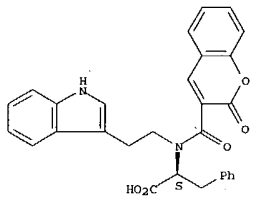
L4 ANSWER 105 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:228654 CAPLUS
DOCUMENT NUMBER: 134:252657
TITLE: Compounds directed against pilus biogenesis and activity in pathogenic bacteria; methods and compositions for synthesis
INVENTOR(S): Kihlberg, Jan; Larsson, Andreas; Svensson, Anette; Fex, Tomas; Hultgren, Scott J.; Pinkner, Jerry
PATENT ASSIGNEE(S): Washington University, USA
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001020995	A1	20010329	WO 2000-US26177	20000922
WO 2001020995	C2	20021114		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 1999-155822P P 19990923
OTHER SOURCE(S): MARPAT 134:252657
AB Many Gram-neg. pathogens assemble adhesive structures on their surfaces that allow them to colonize host tissues and cause disease. Novel compns. which inhibit or prevent the formation of a pilus chaperone-subunit complex are disclosed. Interfering with the function of the pili chaperone neg. affects the chaperone/usher pathway which is one mol. mechanism by which Gram-neg. bacteria assemble adhesive pili structures and thus prevent or inhibit pilus assembly. Also provided are methods for the treatment or prevention of diseases caused by tissue-adhering pilus-forming bacteria by inhibiting the function of pilus chaperones. Also provided are pharmaceutical prepns. capable of inhibiting or preventing the formation of a pilus chaperone-subunit complex. Also provided are methods of synthesizing the N-substituted amino acid compds. and compds. useful for the synthesis thereof. In particular, novel fluorinated linker compds. and methods of synthesis are provided. Methods for using the fluorinated linker compds. in methods of solid-phase synthesis of the N-substituted amino acid compds. are also disclosed. Chiral compds. R4CHR1NR2COR3 [R1-R3 = (un)substituted alkyl, acyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, heterocycloalkyl; R4 = CO2H, CONH2, CHO, B(OH)2, P(O)(OH)2, alkyl or haloalkyl ketone group] and their salts, esters, and amines are claimed. Thus, N-[2-(1H-indol-3-yl)ethyl]-N-(naphthalene-2-carbonyl)tyrosine was prepared and assayed for affinity for periplasmic chaperones PapD and FimC (KD estimated as 1-100μM).
IT **331679-48-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(compds. directed against pilus biogenesis and activity in pathogenic bacteria)
RN 331679-48-2 CAPLUS
CN L-Phenylalanine, N-[2-(1H-indol-3-yl)ethyl]-N-[(2-oxo-2H-1-benzopyran-3-yl)carbonyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 105 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 106 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

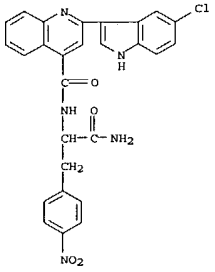
ACCESSION NUMBER: 2001:222008 CAPLUS
DOCUMENT NUMBER: 134:252257
TITLE: Preparation of 2-(indolin-3-yl)quinoline derivatives and compositions in use as antimicrobial agents
INVENTOR(S): Cuny, Gregory D.; Hauske, James R.; Heefner, Donald L.; Hoemann, Michael Z.; Kumaravel, Gnanasambandam; Melikian-Badalian, Anita; Rossi, Richard F.
PATENT ASSIGNEE(S): Sepracor, Inc., USA
SOURCE: U.S., 112 pp., Cont.-in-part of U.S. Ser. No. 878,781, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6207679	B1	20010327	US 1998-45051	19980319
WO 9857931	A2	19981223	WO 1998-US12762	19980618
WO 9857931	A3	19990429		
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, BM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
EP 991623	A2	20000412	EP 1998-930396	19980618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6172084	B1	20010109	US 1998-99640	19980618
JP 2002505689	T2	20020219	JP 1999-504835	19980618
AU 757059	B2	20030130	AU 1998-79797	19980618
US 6103905	A	20000815	US 1998-213385	19981211
NO 9906269	A	20000216	NO 1999-6269	19991217
US 6376670	B1	20020423	US 2000-658690	20000908

PRIORITY APPLN. INFO.:
US 1997-878781 B2 19970619
US 1998-45051 A2 19980319
US 1998-99640 A2 19980618
WO 1998-US12762 W 19980618
US 1998-213385 A1 19981211
US 2000-639622 A2 20000815

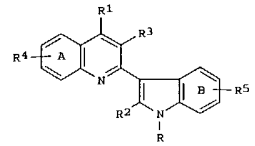
OTHER SOURCE(S): MARPAT 134:252257
GI

L4 ANSWER 106 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 106 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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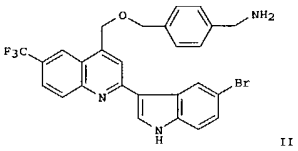


II

AB Title compds. I [wherein; R, R1, R2 and R3 are H, halo, alk(en)(yn)yl, OH, alkoxy, amino, nitro, SH, imine, amide, CO, -(CH2)0-8-R80, etc.; R4 is the same as R-R3 but not H; R5 is the same as R4 except that at least 1(-8) CH2 precede R80; A is (un)substituted with any number of R4 up to the number limited by stability and rules of valence; B is substituted with at least one instance of R5 up to the number limited by stability and rules of valence; R80 is (substituted) aryl, cycloalk(en)yl, heterocyclyl or polycyclyl.] and related quinoline derivs. are prepared as antimicrobial agents. For instance, synthesis of II is accomplished by alkylation of 4-hydroxymethyl-6-trifluoromethyl-2-(N-t-butoxycarbonylindol-3-yl)quinoline with (4-t-butoxycarbonylaminomethyl)benzyl iodide followed by deprotection. There are 282 examples of I provided. The min. inhibitory concentration (MIC) of I against at least one Gram-pos. bacterium is 0.1-10 μg/mL. Certain compds. of formula I have a therapeutic index in primates of at least 10 for the inhibition of infection by at least one Gram-pos. bacterium.

IT **275357-08-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and use of quinolinylindole derivs. as antimicrobial agents)

RN 275357-08-9 CAPLUS
CN 4-Quinolinecarboxamide, N-[2-amino-1-[(4-nitrophenyl)methyl]-2-oxoethyl]-2-(5-chloro-1H-indol-3-yl)- (9CI) (CA INDEX NAME)

L4 ANSWER 107 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

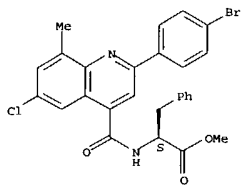
ACCESSION NUMBER: 2001:177411 CAPLUS
DOCUMENT NUMBER: 135:152
TITLE: A series of quinoline analogues as potent inhibitors of C. albicans prolyl tRNA synthetase
AUTHOR(S): Yu, X. Y.; Hill, J. M.; Yu, G.; Yang, Y.; Kluge, A. F.; Keith, D.; Finn, J.; Gallant, P.; Silverman, J.; Lim, A.
CORPORATE SOURCE: Department of Medicinal Chemistry, Cubist Pharmaceuticals, Inc., Cambridge, MA, 02139, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(4), 541-544
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 135:152

AB A series of quinoline inhibitors of C. albicans prolyl tRNA synthetase was identified. The most potent analog, 2-(4-bromophenyl)-6-chloro-8-methyl-4-quinolinecarboxylic acid, showed IC50=5 nM (Ca. ProRS) with high selectivity over the human enzyme.

IT **342018-11-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(a series of quinoline analogs as potent inhibitors of C. albicans prolyl tRNA synthetase)

RN 342018-11-5 CAPLUS
CN L-Phenylalanine, N-[[2-(4-bromophenyl)-6-chloro-8-methyl-4-quinolinyl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 108 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:168124 CAPLUS
DOCUMENT NUMBER: 134:218936
TITLE: Crystal structure of CDC25 proteins and its use in rational design of inhibitors
INVENTOR(S): Taylor, Neil R.; Borhani, David; Epstein, David; Rudolph, Johannes; Ritter, Kurt; Fujimori, Taro; Robinson, Simon; Eckstein, Jens; Haupt, Andreas; Walker, Nigel; Dixon, Richard W.; Choquette, Deborah; Blanchard, Jill; Kluge, Arthur; Pal, Kollol; Bockovich, Nicholas; Come, Jon; Hediger, Mark
PATENT ASSIGNEE(S): Basf Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 314 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

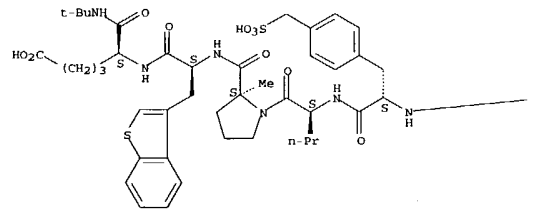
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001016300	A2	20010308	WO 2000-US23473	20000825
WO 2001016300	A3	20020530		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1226237	A2	20020731	EP 2000-959449	20000825
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: US 1999-172215P P 19990831
WO 2000-US23473 W 20000825
OTHER SOURCE(S): MARPAT 134:218936
AB The present invention relates to polypeptides which comprise the ligand binding domain of CDC25, crystalline forms of these polypeptides, and the use of these crystalline forms to determine the 3-dimensional structure of the catalytic domain of CDC25 alone and in complexes with pentapeptide inhibitors. Atomic coordinates are provided from x-ray diffraction of crystals of CDC25A and CDC25B catalytic domains in the presence and absence of various inhibitors. The invention also relates to the use of the 3-dimensional structure of the CDC25 catalytic domain in methods of designing and/or identifying potential inhibitors of CDC25 activity, for example, compds. which inhibit the binding of a native substrate to the CDC25 catalytic domain. The method comprises the steps of (1) identifying one or more functional groups capable of interacting with one or more subsites of the CDC25 catalytic domain, and (2) identifying a scaffold which presents the functional group or functional groups in a suitable orientation for interacting with one or more subsites of the CDC25 catalytic domain. Since CDC25 is a potential target for therapies aimed at controlling proliferative disease, the atomic coordinates allow rational structure-based design of potential agents for the treatment of cancer, restenosis,

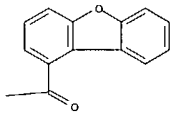
L4 ANSWER 108 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
reocclusion of coronary artery, or inflammation.
IT **329274-06-8P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystal structure of CDC25 proteins and its use in rational design of inhibitors)
RN 329274-06-8 CAPLUS
CN L-Norvalinamide, N-(1-dibenzofuranylcarbonyl)-4-(sulfomethyl)-L-phenylalanyl-L-norvalyl-2-methyl-L-prolyl-3-benzo[b]thien-3-yl-L-alanyl-5-carboxy-N-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

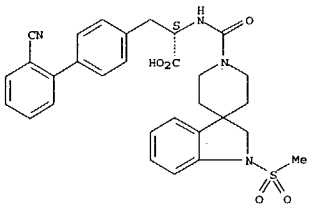


L4 ANSWER 109 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:152640 CAPLUS
DOCUMENT NUMBER: 134:208130
TITLE: Preparation of substituted ureas as cell adhesion inhibitors
INVENTOR(S): Delaszlo, Stephen E.; Hagmann, William K.; Kamenecka, Theodore M.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 60 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014328	A2	20010301	WO 2000-US22437	20000816
WO 2001014328	A3	20020131		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000069093	A5	20010319	AU 2000-69093	20000816
US 6353099	B1	20020305	US 2000-641408	20000817

PRIORITY APPLN. INFO.: US 1999-150055P P 19990820
WO 2000-US22437 W 20000816
OTHER SOURCE(S): MARPAT 134:208130
AB Compds. R1R2NCONR3CR4R5-Y-COR6 [R1, R2 = H, (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, or heteroaryl or R1R2N form a mono- or bicyclic ring; R3 is any group given for R1/R2 or R2 and R3 together with the atoms to which they are attached form a heterocyclic ring with the proviso that R1 and R2 do not form a ring; R4 = (un)substituted alkyl, aryl, arylalkyl, biaryl, biarylalkyl, heteroaryl, heteroarylalkyl, heteroarylaryl, heteroarylarylalkyl, arylheteroaryl, or arylheteroarylalkyl; R5 = H, (un)substituted alkyl, alkenyl, or alkynyl; R6 = OH, alkoxy, alkenoxy, alkynoxy, aryloxy, arylalkoxy, or an amino group; Y is a bond or CR7R8, where R7 = H, alkyl, alkenyl, alkynyl, aryl, or arylalkyl; R8 is any group given for R7 plus OH, alkoxy, halo, NO2, amino, etc.] were prepared as antagonists of VLA-4 and/or α4β7 and are useful in the inhibition or prevention of cell adhesion and cell-adhesion mediated pathologies. Thus, treating 4-(2-methoxyphenyl)-L-phenylalanine tert-Bu ester (obtained from 4-iodo-L-phenylalanine and 2-methoxyphenylboronic acid) with pyrrolidine and p-nitrophenyl chloroformate in CH2Cl2 containing diisopropylethylamine and ester cleavage with 50% TFA/CH2Cl2 afforded N-(1-pyrrolidinylcarbonyl)-4-(2-methoxyphenyl)-L-phenylalanine.
IT **328257-46-1P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of substituted ureas as cell adhesion inhibitors)
RN 328257-46-1 CAPLUS
CN [1,1'-Biphenyl]-4-propanoic acid, 2'-cyano-α-[[[1,2-dihydro-1-(methylsulfonyl)spiro[3H-indole-3,4'-piperidin]-1'-yl]carbonyl]amino]-, (αS)- (9CI) (CA INDEX NAME)

L4 ANSWER 109 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry.

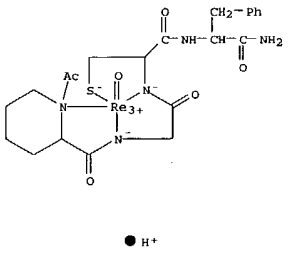


L4 ANSWER 110 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:137478 CAPLUS
DOCUMENT NUMBER: 134:188233
TITLE: Melanocortin metallopeptide constructs, combinatorial libraries, and applications
INVENTOR(S): Sharma, Shubh D.; Shi, Yi-Qun; Yang, Wei; Cai, Hui-Zhi
PATENT ASSIGNEE(S): Palatin Technologies, Inc., USA
SOURCE: PCT Int. Appl., 80 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001013112	A1	20010222	WO 2000-US16396	20000615
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1208377	A1	20020529	EP 2000-944681	20000615
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				

PRIORITY APPLN. INFO.: US 1999-148994P P 19990812
WO 2000-US16396 W 20000615
OTHER SOURCE(S): MARPAT 134:188233
AB Metallopeptides and metallopeptide combinatorial libraries specific for melanocortin receptors are provided, for use in biol., pharmaceutical and related applications. The metallopeptides and combinatorial libraries are made of peptides, peptidomimetics and peptide-like constructs, in which the peptide, peptidomimetic or construct is conformationally fixed on complexation of a metal ion-binding portion thereof with a metal ion.
IT **327605-06-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(melanocortin metallopeptide constructs, combinatorial libraries, and applications)
RN 327605-06-1 CAPLUS
CN Rhenium, [(2R)-1-acetyl-2-piperidinecarbonyl-κN1-glycyl-κN-L-cysteinyl-κN,κS-L-phenylalaninamidato(3-)]oxo-, conjugate monoacid, (SP-5-24)- (9CI) (CA INDEX NAME)

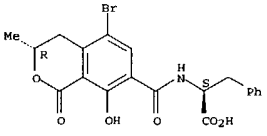
L4 ANSWER 110 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 111 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:111905 CAPLUS
DOCUMENT NUMBER: 134:291367
TITLE: A Kinetic Study into the Hydrolysis of the Ochratoxins and Analogues by Carboxypeptidase A
AUTHOR(S): Stander, Maria A.; Steyn, Pieter S.; van der Westhuizen, Francois H.; Payne, Barry E.
CORPORATE SOURCE: Potchefstroom University for Christian Higher Education, Potchefstroom, S. Afr.
SOURCE: Chemical Research in Toxicology (2001), 14(3), 302-304
CODEN: CRTOEC; ISSN: 0893-228X
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The hydrolyzes of the ochratoxins and analogs by carboxypeptidase A were assessed. This was done by measuring the amount of phenylalanine formed with liquid chromatog. coupled to tandem electrospray mass spectrometry. The kinetic data of ochratoxin A, ochratoxin B, and the synthetic bromo-ochratoxin B were compared to the values of a number of synthesized structure analogs, namely, ochratoxin A Me ester, ochratoxin B Me ester, N-(2-hydroxybenzoyl)phenylalanine, N-(5-chloro-2-hydroxybenzoyl)phenylalanine, N-(5-bromo-2-hydroxybenzoyl)phenylalanine, and N-(5-fluoro-2-hydroxybenzoyl)phenylalanine. The halogen-containing analogs had lower turnovers than their des-halo analogs. There are no substantial differences in the kinetic data between the different halogen-containing analogs.
IT **255042-26-3**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(a kinetic study into the hydrolysis of the ochratoxins and analogs by carboxypeptidase A)
RN 255042-26-3 CAPLUS
CN L-Phenylalanine, N-[[(3R)-5-bromo-3,4-dihydro-8-hydroxy-3-methyl-1-oxo-1H-2-benzopyran-7-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

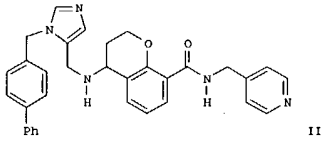


REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 112 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:101132 CAPLUS
DOCUMENT NUMBER: 134:163037
TITLE: Preparation of 4-[(imidazolylmethyl)amino]chroman-8-carboxamides as protein farnesyltransferase inhibitors
INVENTOR(S): Baudoin, Bernard; Jimonet, Patrick; Maignan, Sebastien; Achard, Daniel; Mailliet, Patrick; Laoui, Abdelazize; Nemecek, Conception
PATENT ASSIGNEE(S): Aventis Pharma S.A., Fr.
SOURCE: PCT Int. Appl., 137 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001009125	A1	20010208	WO 2000-FR2188	20000728
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2796947	A1	20010202	FR 1999-9892	19990730

PRIORITY APPLN. INFO.: FR 1999-9892 A 19990730
OTHER SOURCE(S): MARPAT 134:163037
GI



II

AB R1R2NZCONR6CR4R5R10 [I; R1 = Z1Z2Z3Z4R9; R2 = H, alkyl, alkanoyl; R4 = (CHR11)nR14; R5 = H, COR15, Z3R16, Z3OCOR; R4R5 = atoms to complete a ring; R,R11 = H, alkyl, aryl; R6 = H or (hydroxy)alkyl; R4R6 = atoms to complete a ring; R9 = H, halo, alkyl, aryl, etc.; R10 = H or Z3OR; R14 = OR, CO2R, alkyl, (hetero)aryl, etc.; R15 = OH, (alkyl)amino, alkyl, alkoxy; R16 = H, halo, OH; Z = (un)substituted 3,4-dihydro-2H-1-benzopyran-4,8-diyl; Z1,Z3 = alkylene; Z2 = imidazolediyl; Z4 = (hetero)arylene; n = 0-5] were prepared Thus, 4-chromanone was converted in 3 steps to 4-(Bocamino)chroman-8-carboxylic acid which was amidated by 4-pyridinemethanamine and the chromatog. resolved product deprotected to give (-)- and (+)-4-amino-N-(4-pyridylmethyl)chroman-8-carboxamide. The latter enantiomer was reductively condensed with 1-

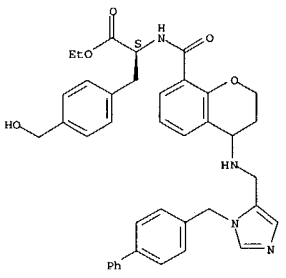
L4 ANSWER 112 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
biphenylylmethylimidazole-5-carboxaldehyde (prepn. given) to give title compd. (+)-II. Data for biol. activity of I were given.

IT **325151-75-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-[(imidazolylmethyl)amino]chroman-8-carboxamides as protein farnesyltransferase inhibitors)

RN 325151-75-5 CAPLUS

CN L-Phenylalanine, N-[[4-[[[1-([1,1'-biphenyl]-4-ylmethyl)-1H-imidazol-5-yl]methyl]amino]-3,4-dihydro-2H-1-benzopyran-8-yl]carbonyl]-4-(hydroxymethyl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



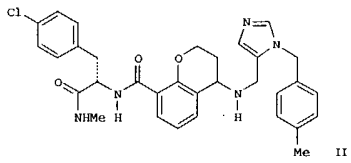
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 113 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:101131 CAPLUS
DOCUMENT NUMBER: 134:163036
TITLE: Preparation of 4-[(imidazolylmethyl)amino]chroman-8-carboxamides as protein farnesyl transferase inhibitors
INVENTOR(S): Baudoin, Bernard; Jimonet, Patrick
PATENT ASSIGNEE(S): Aventis Pharma S.A., Fr.
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001009124	A1	20010208	WO 2000-FR2187	20000728
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
FR 2796946	A1	20010202	FR 1999-9891	19990730

PRIORITY APPLN. INFO.: FR 1999-9891 A 19990730
OTHER SOURCE(S): MARPAT 134:163036
GI



II

AB R9C6H4CH2ZCH2NR2Z1CONHCH(CH2R4)CONHMe [I; R2 = H, alkyl, alkanoyl; R4 = (un)substituted aryl; R9 = halo, alkyl, (hetero)aryl, Z2COR12, etc.; R12 = OH, alkoxy, NH2; Z = imidazole-1,5-diyl; Z1 = (un)substituted 3,4-dihydro-2H-1-benzopyran-4,8-diyl; Z2 = alkylene] were prepared Thus, 4-chromanone was converted in 3 steps to 4-(t-Boc-amino)chroman-8-carboxylic acid which was amidated by (S)-4-ClC6H4CH(NH2)CO2Me and the product amidated by MeNH2 to give, after deprotection, 4-amino-N-[(S)-1-methylcarbamoyl-2-(4-chlorophenyl)ethyl]chroman-8-carboxamide. The latter was reductively condensed with 1-(4-methylbenzyl)imidazole-5-carboxaldehyde (preparation given) to give title

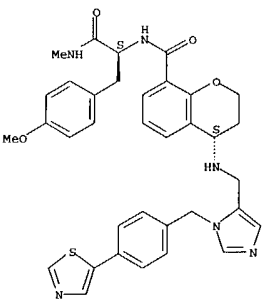
L4 ANSWER 113 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
compd. (+)-II. Data for biol. activity of I were given.

IT **325144-37-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-[(imidazolylmethyl)amino]chroman-8-carboxamides as protein farnesyltransferase inhibitors)

RN 325144-37-4 CAPLUS

CN 2H-1-Benzopyran-8-carboxamide, 3,4-dihydro-N-[(1S)-1-[(4-methoxyphenyl)methyl]-2-(methylamino)-2-oxoethyl]-4-[[[1-[[4-(5-thiazolyl)phenyl]methyl]-1H-imidazol-5-yl]methyl]amino]-, (4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



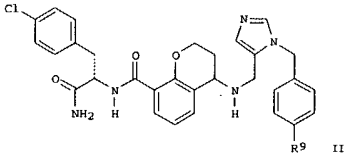
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 114 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2001:101119 CAPLUS
DOCUMENT NUMBER: 134:163035
TITLE: Preparation of 4-[(imidazolylmethyl)amino]chroman-8-carboxamides as protein farnesyltransferase inhibitors
INVENTOR(S): Baudoin, Bernard; Jimonet, Patrick; Laoui, Abdelazize
PATENT ASSIGNEE(S): Aventis Pharma S.A., Fr.
SOURCE: PCT Int. Appl., 54 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001009112	A1	20010208	WO 2000-FR2189	20000728
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
FR 2796948	A1	20010202	FR 1999-9895	19990730

PRIORITY APPLN. INFO.: FR 1999-9895 A 19990730
OTHER SOURCE(S): MARPAT 134:163035
GI



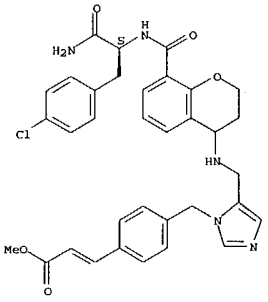
II

AB R9C6H4CH2ZCH2NR2Z1CONHCHR4R5 [I; R2 = H, alkyl, alkanoyl; R4 = CHR13R14; R5 = COR15; R9 = Z2Z3R12; R12,R15 = OH, alkoxy, NH2; R13,R14 = H or (un)substituted aryl; Z = imidazole-1,5-diyl; Z1 = (un)substituted 3,4-dihydro-2H-1-benzopyran-4,8-diyl; Z2 = alk(en)ylene; Z3 = bond or CO] were prepared Thus, 4-chromanone was converted in 3 steps to 4-(Bocamino)chroman-8-carboxylic acid which was amidated by (S)-4-ClC6H4CH(NH2)CO2Me and the product amidated by NH3 to give, after deprotection, 4-amino-N-[(S)-1-carbamoyl-2-(4-chlorophenyl)ethyl]chroman-8-carboxamide. The latter was reductively condensed with 1-[4-(2-methoxycarbonylvinyl)benzyl]imidazole-5-carboxaldehyde (preparation given) to give title compound (+)-II (R9 = CH:CHCO2Me). Data for biol. activity of I were given.

IT **324806-29-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

L4 ANSWER 114 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 4-[(imidazolylmethyl)amino]chroman-8-carboxamides as protein farnesyltransferase inhibitors)
RN 324806-29-3 CAPLUS
CN 2-Propenoic acid, 3-[4-[[5-[[[8-[[[(1S)-2-amino-1-[(4-chlorophenyl)methyl]-2-oxoethyl]amino]carbonyl]-3,4-dihydro-2H-1-benzopyran-4-yl]amino]methyl]-1H-imidazol-1-yl]methyl]phenyl]-, methyl ester (9CI) (CA INDEX NAME)

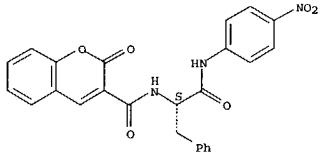
Absolute stereochemistry.
Double bond geometry unknown.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 115 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:2798 CAPLUS
DOCUMENT NUMBER: 134:193689
TITLE: Synthesis and fluorescence properties of intramolecularly quenched fluorogenic p-nitroanilides containing coumarin or quinolinone derivatives as fluorophores
AUTHOR(S): Charitos, C.; Tzougraki, C.; Kokotos, G.
CORPORATE SOURCE: Department of Chemistry, University of Athens, Athens, 157 71, Greece
SOURCE: Journal of Peptide Research (2000), 56(6), 373-381
CODEN: JPERFA; ISSN: 1397-002X
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:193689
AB Nine model intramolecularly quenched fluorogenic substrates (IQFS) of the general structure F-Phe-NH-Np, containing coumarin or quinolinone derivs. as fluorophores (F) and the p-nitroanilide group (Np) as quencher, were synthesized. The study of the fluorescence properties of the substrates synthesized and the corresponding fluorophores showed that efficient quenching of fluorescence (>89%) was observed in all cases. The combination of 7-glutarylamido-4-methyl-coumarin (Mec-NH-Glt-OH) or 7-methoxy-4-coumarylacetic acid (Mca) with the p-nitroanilide group gave the best results (97.2 and 98.8% quenching, resp.). These fluorophores can be used to convert peptide p-nitroanilides into IQFS, which, retaining their chromogenic properties, may be applied in both fluorometric and colorimetric assays.
IT **182944-07-6P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(preparation and fluorescence properties of fluorogenic nitroanilides containing coumarin or quinolinone derivs. as fluorophores)
RN 182944-07-6 CAPLUS
CN 2H-1-Benzopyran-3-carboxamide, N-[(1S)-2-[(4-nitrophenyl)amino]-2-oxo-1-(phenylmethyl)ethyl]-2-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



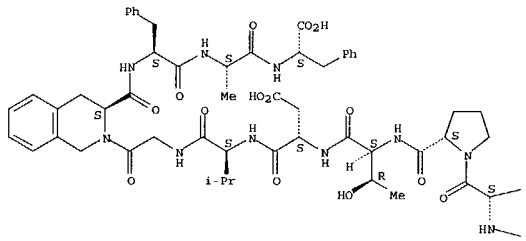
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 116 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:894620 CAPLUS
DOCUMENT NUMBER: 134:141358
TITLE: Development of the first CGRP-antagonist with nanomolar affinity
AUTHOR(S): Beck-Sickinger, Annette G.; Rist, Beate; Enzeroth, Michael; Lacroix, Silvain
CORPORATE SOURCE: Department of Pharmacy, ETH Zurich, Zurich, CH 8057, Switz.
SOURCE: Peptides for the New Millennium, Proceedings of the American Peptide Symposium, 16th, Minneapolis, MN, United States, June 26-July 1, 1999 (2000), Meeting Date 1999, 222-223. Editor(s): Fields, Gregg B.; Tam, James P.; Barany, George. Kluwer Academic Publishers: Dordrecht, Neth.
CODEN: 69ATHX
DOCUMENT TYPE: Conference
LANGUAGE: English
AB CGRP 27-37, which binds to human CGRP1-receptors with low affinity, has been systematically varied. In a stepwise rational optimization the undecapeptides FVPTNVGPFAF and FVPTDVGPFAF have been identified, which bind to human CGRP-receptors. The replacement of Ser34 by Pro has turned out to be crucial for the increase of affinity. Interestingly, neither hydroxyproline (Hyp), nor homoproline (Hpr) could fully replace Pro34, whereas Aib and Tic were only slightly less active. The increase of affinity of single mutations has been additive and correlated with the decrease of the min. at λ = 220 nm by CD spectroscopy. FVPTDVGPFAF and FVPTNVGPFAF showed exclusively antagonistic properties in the rat vasodilatation assay. Interestingly, the duration of the potency of both compds. varied significantly. Whereas FVPTDVGPFAF lost potency after 30 min, analogs with replacement of Asp31 by Asn31 were active for more than 2 h. Since both ligands exhibit receptor binding affinities in the same range (Ki = 19/14 nM), the authors suggested that the analog with Asp31 is more rapidly metabolized, perhaps because of an increased susceptibility for proteases. This effect could be confirmed by preliminary results with other analogs containing either Asp or Asn in position 31. In this case as well, the effect of the Asp containing peptides was significantly increased. This suggests differences in the metabolism of both compds. and could be important for drug design.
IT **324035-60-1**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(development of first CGRP-antagonist with nanomolar affinity)
RN 324035-60-1 CAPLUS
CN L-Phenylalanine, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-α-asparty-L-valylglycyl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

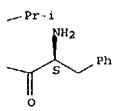
Absolute stereochemistry.

L4 ANSWER 116 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

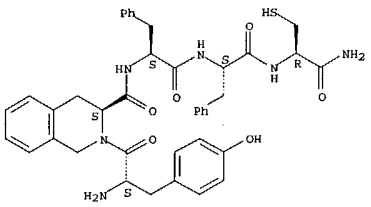
L4 ANSWER 117 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:893936 CAPLUS
DOCUMENT NUMBER: 134:141891
TITLE: Binding and internalization of fluorescent opioid peptide conjugates in living cells
AUTHOR(S): Arttamangkul, Seksiri; Alvarez-Maubecin, Veronica; Thomas, Gerald; Williams, John T.; Grandy, David K.
CORPORATE SOURCE: Department of Physiology and Pharmacology and Vollum Institute for Advanced Biomedical Research, Oregon Health Sciences University, Portland, OR, USA
SOURCE: Molecular Pharmacology (2000), 58(6), 1570-1580
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The dynamics of agonist-stimulated opioid receptor internalization and trafficking have been difficult to study in living cells in part because the available probes were inadequate. To overcome this obstacle, six new fluorescent opioid peptides were developed. Dermorphin (DERM), deltorphin (DELT), TIPP, and endomorphin were conjugated to BODIPY TR or Alexa Fluor 488, two fluorescent dyes with distinct hydrophobic properties. In membrane binding assays the fluorescent conjugates DERM-A488 or -BTR, DELT-A488 or -BTR, and TIPP-A488 displayed good binding affinity and selectivity for μ- and δ-opioid receptor subtypes. Furthermore, the fluorescent conjugates of dermorphin and deltorphin were biol. active as demonstrated by their ability to hyperpolarize locus coeruleus neurons (DERM-A488 or -BTR) and inhibit calcium currents in NG108-15 (DELT-A488). Both of these responses were antagonized by naloxone. In conjunction with confocal fluorescent microscopy the trafficking of these fluorescent ligands was monitored in real-time. The internalization of these ligands by μ- and δ-opioid receptors was found to be naloxone-sensitive and temperature-dependent. Interestingly, once these ligands were internalized the fluorescent puncta that formed became distributed in one of two patterns. In Chinese hamster ovary cells heterologously expressing either μ- or δ-opioid receptors the intracellular puncta were concentrated in the perinuclear region of the cell, whereas they were distributed throughout the cytoplasm in cells derived from either NG108-15 or SH-SY5Y cells. In summary, we have demonstrated that these novel, fluorescent opioid peptide conjugates permit real-time visual tracking of receptor-ligand complexes, including their internalization and trafficking, in living cells.

IT **322475-56-9DP**, conjugates with Alexa Fluor 488 and Bodipy TR
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); PNU (Preparation, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(binding and internalization of fluorescent opioid peptide conjugates in living cells coupled with functional activation)
RN 322475-56-9 CAPLUS
CN L-Cysteinamide, L-tyrosyl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-phenylalanyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 117 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



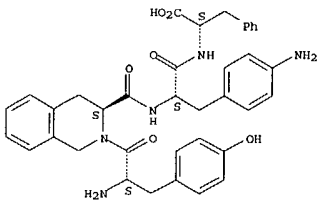
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 118 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:832189 CAPLUS
DOCUMENT NUMBER: 134:116218
TITLE: Synthesis and evaluation of isothiocyanate-containing derivatives of the δ-opioid receptor antagonist Tyr-Tic-Phe-Phe (TIPP) as potential affinity labels for δ-opioid receptors
AUTHOR(S): Maeda, Dean Y.; Berman, Fred; Murray, Thomas F.; Aldrich, Jane V.
CORPORATE SOURCE: Department of Pharmaceutical Sciences School of Pharmacy, University of Maryland, Baltimore, MD, 21201, USA
SOURCE: Journal of Medicinal Chemistry (2000), 43(26), 5044-5049
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 134:116218

AB Derivs. of the δ-opioid receptor-selective peptide antagonist H-Tyr-Tic-Phe-Phe-OH (TIPP) containing an isothiocyanate moiety at the para position of either Phe3 or Phe4 were prepared as potential affinity labels for δ-opioid receptors. The synthesis was accomplished using a general solution-phase synthetic procedure, which allows for the introduction of affinity labeling groups late in the synthesis of a variety of small peptide substrates. The target peptides and their corresponding amines were then evaluated in radioligand binding expts. using Chinese hamster ovary (CHO) cells expressing δ- and μ-opioid receptors. The peptides [Phe(p-NCS)3]TIPP (2) and [Phe(p-NCS)4]TIPP (4) showed affinity for δ-receptors comparable to the parent compound TIPP (IC50 = 12 and 5 nM, resp., vs. 6 nM for TIPP). Both peptides 2 and 4 were able to inhibit radioligand binding to δ-receptors in a wash-resistant manner at a concentration of 10 nM.

IT **320782-32-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. evaluation of isothiocyanate-containing TIPP analogs as
antagonists of the δ-opioid receptor)
RN 320782-32-9 CAPLUS
CN L-Phenylalanine, L-tyrosyl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-4-amino-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 118 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 119 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:830796 CAPLUS
DOCUMENT NUMBER: 134:101182
TITLE: Extended TIP(P) analogs as precursors for labeled δ-opioid receptor ligands
AUTHOR(S): Kumar, Vivek, Murray, Thomas F.; Aldrich, Jane V.
CORPORATE SOURCE: Department of Pharmaceutical Sciences School of Pharmacy, University of Maryland, Baltimore, MD, 21201, USA
SOURCE: Journal of Medicinal Chemistry (2000), 43(26), 5050-5054
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

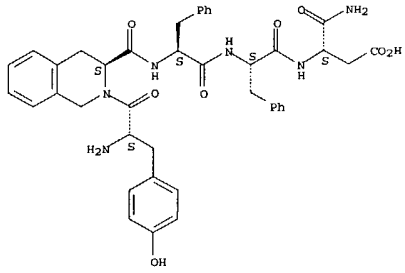
AB Peptides H-Tyr-Tic-Phe-Phe-OH (TIPP) and the shorter H-Tyr-Tic-Phe-OH (TIP) are potent and highly selective antagonists at the δ-opioid receptor and, therefore, are ideal candidates for the attachment of labels to assist in the study of δ-opioid receptors. Peptides extended at the C-terminus with residues (i.e., Asp, Asn, Glu, Gln and Lys, which can be used as handles for further modification and/or labeling) were synthesized. The TIPP-D/L-Asx/Glx derivs. (Asx = Asp or Asn; Glx = Glu or Gln) exhibited similar δ-receptor affinity to TIPP (Ki ≈ 5-10 nM vs Ki = 6 nM), and neither the location of the carboxylic acid moiety nor the stereochem. of the C-terminal residue significantly affected the δ-receptor affinity of these derivs. Extension of TIPP with an addnl. residue did not increase μ-receptor affinity, even though the position of the acidic group, which imparts δ-receptor selectivity to TIPP, was shifted relative to the carboxylic acid moiety of TIPP. The δ-receptor affinities of the TIP-D/L-Asx/Glx derivs. were found to be influenced mainly by the position of the carboxylic acid function rather than the stereochem. of the C-terminal residue. TIP(P)-D/L-Lys(Ac)-OH derivs. exhibited moderate δ-receptor affinity (Kiδ = 16-28 nM). The most potent compds. found in the extended TIP(P) series were TIPP-D-Gln-OH and TIP-D-Gln-OH (Kiδ ≈ 5 nM), which had similar affinities to TIPP.

IT **319906-09-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of TIP(P) analogs, extended at the C-terminus, as precursors for labeled δ-opioid receptor ligands)

RN 319906-09-7 CAPLUS
CN L-α-Asparagine, L-tyrosyl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-phenylalanyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 119 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

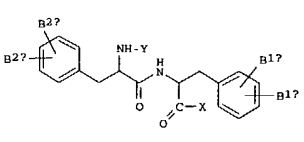
L4 ANSWER 120 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:824283 CAPLUS
DOCUMENT NUMBER: 134:5161
TITLE: Preparation of phosphonic and carboxylic acid derivatives as inhibitors of protein tyrosine phosphatase-1B (PTP-1B)
INVENTOR(S): LeBlanc, Yves; Dufresne, Claude; Roy, Patrick; Wang, Zhaoyin
PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000069889	A1	20001123	WO 2000-CA567	20000512
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1181309	A1	20020227	EP 2000-929175	20000512
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6365592	B1	20020402	US 2000-570092	20000512

PRIORITY APPLN. INFO.: US 1999-134150P P 19990514
US 1999-158778P P 19991012
WO 2000-CA567 W 20000512

OTHER SOURCE(S): MARPAT 134:5161
GI



I

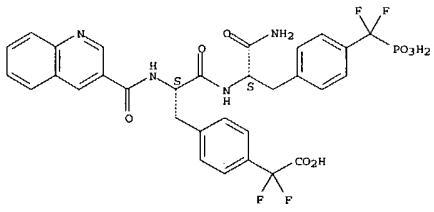
AB Peptides I [B1a, B1b, B2a, B2b = CF2PO3H2 or CF2CO2H or one of B1a, B1b, B2a, and B2b is H and the others are H, alkyl, heteroaryl, carbocyclyl, aryl, OH, halo, CHF2, CF3, CHFCO2H, CH2PO3H2, SO2NH2, etc.; X = OH, NH2; Y = H, alkyl, R1-Z-CO (R1 = alkyl, fluoroalkyl, aryl, heteroaryl, etc.; Z = O, SCH2, SOCH2, SO2CH2, substituted imino, or CH:CH), acyl residue of an amino acid which may be substituted, alkyl- or arylsulfonyl] were prepared as inhibitors of PTP-1B. Thus, (4S)-5-[(1S)-2-[[(1S)-2-amino-1-[4-[difluoro(phosphono)methyl]benzyl]-2-oxoethyl]amino]-1-[[4-(carboxydifluoromethyl)benzyl]-2-oxoethyl]amino]-4-(benzoylamino)-5-oxopentanoic acid was prepared by the solid-phase method using a TentaGel RAM resin.

L4 ANSWER 120 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

IT **307990-98-3P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phosphonic and carboxylic acid derivs. as inhibitors of protein tyrosine phosphatase-1B)

RN 307990-98-3 CAPLUS
CN L-Phenylalaninamide, 4-(carboxydifluoromethyl)-N-(3-quinolinylcarbonyl)-L-phenylalanyl-4-(difluorophosphonomethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



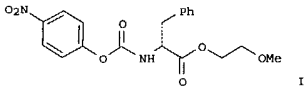
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 121 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:755247 CAPLUS
DOCUMENT NUMBER: 133:322122
TITLE: Enantiopure reagents and process for the separation of amino acid enantiomers
INVENTOR(S): Delplanche, Thierry; Callens, Roland
PATENT ASSIGNEE(S): Solvay (Societe Anonyme), Belg.
SOURCE: Eur. Pat. Appl., 18 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1046627	A2	20001025	EP 2000-201285	20000410
EP 1046627	A3	20001102		
EP 1046627	B1	20040211		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BE 1012622	A3	20010109	BE 1999-280	19990421
AT 259339	E	20040215	AT 2000-201285	20000410
CA 2305944	AA	20001021	CA 2000-2305944	20000418
JP 2000327594	A2	20001128	JP 2000-120313	20000421

PRIORITY APPLN. INFO.: BE 1999-280 A 19990421
GI



I

AB Enantiopure reagents, e.g. I, were prepared and used in resolution of racemic amino acids in presence of NEt3.

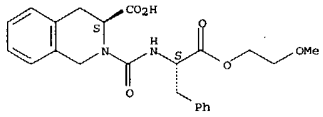
IT **302837-74-7P**
RL: PUR (Purification or recovery); SPN (Synthetic preparation); PREP (Preparation)
(preparation of enantiopure reagents and process for the resolution of amino acids)

RN 302837-74-7 CAPLUS

CN 3-Isoquinolinecarboxylic acid, 1,2,3,4-tetrahydro-2-[[[(1S)-2-(2-methoxyethoxy)-2-oxo-1-(phenylmethyl)ethyl]amino]carbonyl]-, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 121 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 122 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:752379 CAPLUS
DOCUMENT NUMBER: 134:50988
TITLE: Chiral Resolution, Pharmacological Characterization, and Receptor Docking of the Noncompetitive mGlu1 Receptor Antagonist (±)-2-Hydroxyimino-1a,2-dihydro-1H-7-oxacyclopropa[b]naphthalene-7a-carboxylic Acid Ethyl Ester
AUTHOR(S): Ott, David; Floersheim, Philipp; Inderbitzin, Werner; Stoehr, Natacha; Francotte, Eric; Lecis, Gabrielle; Richert, Paul; Rihs, Grety; Flor, Peter Josef; Kuhn, Rainer; Gasparini, Fabrizio
CORPORATE SOURCE: Nervous System Research and Core Technologies, Novartis Pharma AG, Basel, CH-4002, Switz.
SOURCE: Journal of Medicinal Chemistry (2000), 43(23), 4428-4436
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Racemic CPCCOEt ((1aRS,7aRS)-2-hydroxyimino-1a,2-dihydro-1H-7-oxacyclopropa[b]naphthalene-7a-carboxylic acid Et ester, (±)-1) derivs. have been shown to be subtype-selective metabotropic glutamate (mGlu) 1 receptor antagonists (Annoura et al. Bioorg. Med. Chemical Lett. 1996, 6, 763-766). The optical isomers of (±)-1 have been separated by chromatog. on a chiral stationary phase. The absolute configuration at the C-1a and C-7a positions was determined using x-ray crystallog. of an amide derivative with the Me ester of L-phenylalanine (L-PheOMe) ((+)-6). In a phosphoinositol (PI) turnover assay at the cloned human mGlu1b receptor, (-)-1 and the new amide derivs. (-)-5 and (-)-6, all of which have (1aS,7aS)-stereochem. on the chromane ring system, showed IC50 values of 1.5, 0.43, and 0.93 μM, resp. In contrast, (+)-1 and the new amide derivs. (+)-5 and (+)-6 were found to be inactive up to a concentration of 30 μM indicating a selectivity for the (-)-enantiomers of at least 70-fold. In a previous study (Litschig et al. Mol. Pharmacol. 1999, 55, 453-461) we demonstrated using site-directed mutagenesis that the interaction site of (±)-1 is located in the transmembrane (TM) domain of hmGlu1b. To suggest a plausible binding mode of (-)-1, we have built a mol. mechanics model of the putative seven TM domain of hmGlu1 based on the α-carbon template of the TM helixes of rhodopsin. A receptor docking hypothesis suggests that the OH of T815 (TMVII) comes in close contact with the oxime OH of (-)-1 and (-)-5, whereas no such close interactions could be demonstrated by docking of (+)-1.

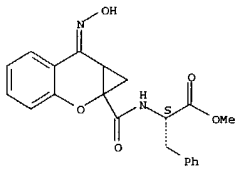
IT **314021-52-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(chiral resolution, pharmacol. characterization, and receptor docking of the noncompetitive mGlu1 receptor antagonist (±)-2-hydroxyimino-1a,2-dihydro-1H-7-oxacyclopropa[b]naphthalene-7a-carboxylic acid Et ester)

RN 314021-52-8 CAPLUS

CN L-Phenylalanine, N-[[7,7a-dihydro-7-(hydroxyimino)benzo[b]cyclopropa[e]pyran-1a(1H)-yl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

L4 ANSWER 122 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

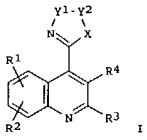


REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 123 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:707159 CAPLUS
DOCUMENT NUMBER: 133:266851
TITLE: Preparation of 4-(imidazolin-2-yl)quinolines as NK-3 and/or GABAA receptor ligands
INVENTOR(S): Yuan, Jun; Maynard, George D.; Hutchison, Alan; Rachwal, Stanislaw
PATENT ASSIGNEE(S): Neurogen Corporation, USA
SOURCE: PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000058303	A1	20001005	WO 2000-US8205	20000328
WO 2000058303	C2	20021219		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1165542	A1	20020102	EP 2000-919753	20000328
EP 1165542	B1	20030820		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6413982	B1	20020702	US 2000-536922	20000328
JP 2002540203	T2	20021126	JP 2000-608005	20000328
AT 247652	E	20030915	AT 2000-919753	20000328
US 2002198232	A1	20021226	US 2002-140693	20020507
US 6624175	B2	20030923		

PRIORITY APPLN. INFO.: US 1999-126926P P 19990329
US 2000-536922 A1 20000328
WO 2000-US8205 W 20000328
OTHER SOURCE(S): MARPAT 133:266851
GI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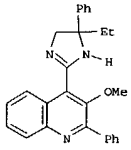
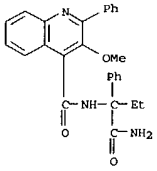

II

L4 ANSWER 123 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
AB The title compds. [I; R1 = H, halo, OH, etc.; R2, R3 = (un)substituted alkyl, Ph, naphthyl, etc.; R4 = H, halo, OH, etc.; X = NH, O, N(alkyl); Y1 = CR11R12, CR11R12(CH2)p, (CH2)pCR11R12, (CH2)pCO (wherein p = 0-2; R11, R12 = H, (un)substituted Ph, naphthyl, etc.); Y2 = CR11R12, CO (with the proviso that Y2 is not CO when Y1 = (CH2)pCO)] which bind with high affinity to NK-3 receptors and/or GABAA receptors, and therefore are useful in treating patients suffering from certain central nervous system and peripheral diseases or disorders, were prepared E.g., a multi-step synthesis of imidazoline II which showed IC50 of 19 nM against NK-3 receptor binding, was given. This invention also relates to the use of compds. I in combination with one or more other CNS agents to potentiate the effects of the other CNS agents. The compds. I are also useful as probes for the localization of NK-3 receptors and GABAA receptors.
IT **298689-34-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of 4-(imidazolin-2-yl)quinolines as NK-3 and/or GABAA receptor ligands)
RN 298689-34-6 CAPLUS
CN 4-Quinolinecarboxamide, N-[1-(aminocarbonyl)-1-phenylpropyl]-3-methoxy-2-phenyl- (9CI) (CA INDEX NAME)

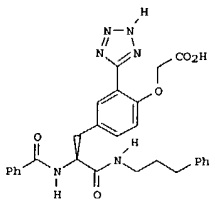


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 124 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:645993 CAPLUS
DOCUMENT NUMBER: 133:238324
TITLE: Preparation of tyrosine amides and analogs as protein tyrosine phosphatase inhibitors
INVENTOR(S): Larsen, Scott D.; May, Paul D.; Bleasdale, John E.; Liljebris, Charlotta; Schostarez, Heinrich Josef; Barf, Tjeerd; Nilsson, Marianne
PATENT ASSIGNEE(S): Pharmacia and Upjohn AB, Swed.
SOURCE: PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000053583	A1	20000914	WO 2000-US6022	20000309
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6410585	B1	20020625	US 1999-265410	19990310
EP 1161421	A1	20011212	EP 2000-917793	20000309
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002539115	T2	20021119	JP 2000-604023	20000309

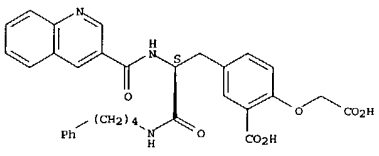
PRIORITY APPLN. INFO.: US 1999-265410 A 19990310
US 1997-57730P P 19970828
US 1998-138642 A2 19980824
WO 2000-US6022 W 20000309
OTHER SOURCE(S): MARPAT 133:238324
GI


II

AB RZCH2CR1R2NHZ1R3 [I; R = OSO3H, OCH2CO2R4, OCH2CONHOH, N(CH2CO2R4)2, etc.;

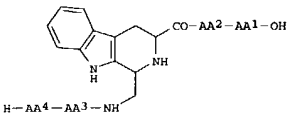
L4 ANSWER 124 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
R1 = H, CH2OH, alkylcarbamoyl, etc.; R2 = H or Me; R4 = H or (phenyl)alkyl; Z = (un)substituted 1,4-phenylene; Z1 = CO or SO2] were prepd. Thus, (S)-Me2CO2CNHCH(CO2H)CH2C6H3(OH)I-4,3 was amidated by Ph(CH2)4NH2 and the product converted in 5 steps to title compd. II. Data for biol. activity of I were given.
IT **292834-82-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tyrosine amides and analogs as protein tyrosine phosphatase inhibitors)
RN 292834-82-3 CAPLUS
CN Benzoic acid, 2-(carboxymethoxy)-5-[(2S)-3-oxo-3-[(4-phenylbutyl)amino]-2-[(3-quinolinylcarbonyl)amino]propyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 125 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:609236 CAPLUS
DOCUMENT NUMBER: 133:310131
TITLE: Solid-phase synthesis of 1,2,3,4-tetrahydro-β-carboline-containing peptidomimetics
AUTHOR(S): Li, Xianfeng; Zhang, Lianshan; Zhang, Wei; Hall, Steven E.; Tam, James P.
CORPORATE SOURCE: Sphinx Pharmaceuticals A Division of Eli Lilly and Company, Cambridge, MA, 02139, USA
SOURCE: Organic Letters (2000), 2(20), 3075-3078
CODEN: ORLEF7; ISSN: 1523-7060
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:310131
GI



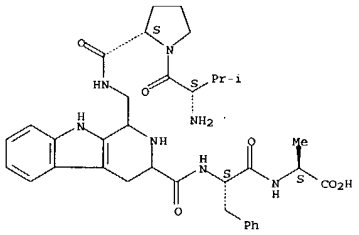
I

AB A solid-phase method for the synthesis of 1,2,3,4-tetrahydro-β-carboline-containing peptidomimetics I (AA1-AA4 = Ala, Leu, Phe, Pro, Val, Asp, Gly, etc.) has been developed. The key step in the strategy is the Pictet-Spengler condensation of a resin-bound tryptophan-containing fragment with an Fmoc-amino aldehyde.

IT **301850-18-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid-phase synthesis of tetrahydro-β-carboline-containing peptidomimetics)
RN 301850-18-0 CAPLUS
CN L-Alanine, 2,3,4,9-tetrahydro-1-[[(L-valyl-L-prolyl)amino]methyl]-1H-pyrido[3,4-b]indole-3-carbonyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 125 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 126 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:568542 CAPLUS
DOCUMENT NUMBER: 133:150464
TITLE: Preparation of quinolinylindole derivatives and compositions in use as antimicrobial agents
INVENTOR(S): Cuny, Gregory D.; Hauske, James R.; Heefner, Donald L.; Hoemann, Michael Z.; Kumaravel, Gnanasambandam; Melikian-Badalian, Anita; Rossi, Richard F.; Xie, Roger L.
PATENT ASSIGNEE(S): Sepracor, Inc., USA
SOURCE: U.S., 228 pp., Cont.-in-part of U.S. Ser. No. 99,640.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6103905	A	20000815	US 1998-213385	19981211
US 6207679	B1	20010327	US 1998-45051	19980319
US 6172084	B1	20010109	US 1998-99640	19980618
WO 2000034265	A2	20000615	WO 1999-US28744	19991203
WO 2000034265	A3	20021003		

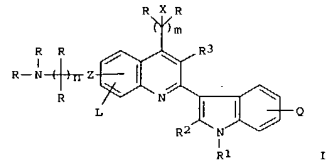
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

US 6376670	B1	20020423	US 2000-658690	20000908

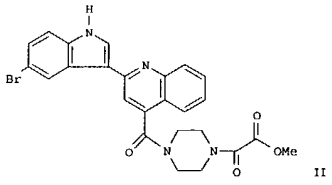
PRIORITY APPLN. INFO.:
US 1997-878781 B2 19970619
US 1998-45051 A2 19980319
US 1998-99640 A2 19980618
US 1998-213385 A 19981211
US 2000-639622 A2 20000815

OTHER SOURCE(S): MARPAT 133:150464
GI

L4 ANSWER 126 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



I

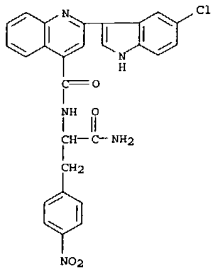


II

AB Title compds. [I; Q = hydrophobic group, H; X = heterocyclyl, amidinyl, formamidonyl, guanidinyl, CN, CSNR2, OR, SR; Z = CC, (E)-CH:CH, (Z)-CH:CH, (CH2)2; L = hydrophobic group, H; R represents independently for each occurrence = H, alkyl, heteroalkyl, aryl, heteroaryl, acyl, sulfonyl; R1 = H, alkyl, aryl, 4-CH3C6H4SO2, (CH2)d; d = 1-6; R2 = H, alkyl, aryl; R3 = H, alkyl, aryl; m = 1-8; n = 1-4] and pharmaceutical prepns. using title compds. are prepared as antimicrobial agents. The MIC value of I against at least one Gram-pos. bacterium ranged from 0.1-10 μg/mL. Thus, the title compound II was prepared and has a therapeutic index in primates of at least 10 for the inhibition of infection by at least one Gram-pos. bacterium.

IT **275357-08-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of quinolinylindole derivs. as antimicrobial agents)
RN 275357-08-9 CAPLUS
CN 4-Quinolinecarboxamide, N-[2-amino-1-[(4-nitrophenyl)methyl]-2-oxoethyl]-2-(5-chloro-1H-indol-3-yl)- (9CI) (CA INDEX NAME)

L4 ANSWER 126 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



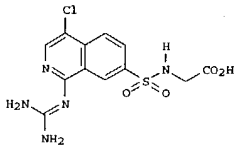
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 127 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:508920 CAPLUS
DOCUMENT NUMBER: 133:120243
TITLE: Preparation of guanidinoisoquinolines as urokinase inhibitors
INVENTOR(S): Dickinson, Roger Peter; Fish, Paul Vincent; Barber, Christopher Gordon
PATENT ASSIGNEE(S): UK
SOURCE: U.S., 94 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6093731	A	20000725	US 1999-359439	19990722
PRIORITY APPLN. INFO.:			US 1999-359439	19990722

OTHER SOURCE(S): MARPAT 133:120243
GI



I

AB RZZ2NR2Z1R3 [R = N:C(NH2)2 or NHC(:NH)NH2; R2 = H, alkyl, (hetero)aryl, etc.; R3 = CO2H, alkoxycarbonyl, CH2OH,CONH2, CH2NH2, etc.; Z = (4-halo)isoquinoline-1,7-diyl; Z1 = (un)substituted (hetero)(cyclo)alkylene or (un)substituted arylene; Z2 = CO, CH2, SO2] were prepared as urokinase inhibitors (no data). Thus, 1,4-dichloroisoquinoline-7-sulfonyl chloride (preparation given) was amidated by H2NCH2CO2CMe3 and the product condensed with guanidine to give, after saponification, title compd I.

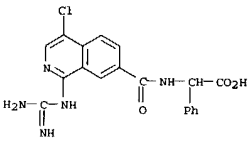
IT **256476-58-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of guanidinoisoquinolines as urokinase inhibitors)

RN 256476-58-1 CAPLUS
CN Benzeneacetic acid, α-[[[1-[(aminoiminomethyl)amino]-4-chloro-7-isoquinolinyl]carbonyl]amino]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

L4 ANSWER 127 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

CRN 256476-57-0
CMF C19 H16 Cl N5 O3



CM 2

CRN 76-05-1
CMF C2 H F3 O2

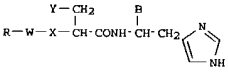
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 128 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:501827 CAPLUS
DOCUMENT NUMBER: 133:120332
TITLE: Preparation of histamines as inhibitors of protein geranylgeranyl transferase I for use of antifungal agents
INVENTOR(S): Okubo, Mitsuru; Ono, Jun; Asahi, Shuichi; Sagara, Takeshi; Sato, Toshihiko; Morishima, Hajime
PATENT ASSIGNEE(S): Banyu Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 15 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2000204078	A2	20000725	JP 1999-5249	19990112
PRIORITY APPLN. INFO.:			JP 1999-5249	19990112

OTHER SOURCE(S): MARPAT 133:120332
GI



I

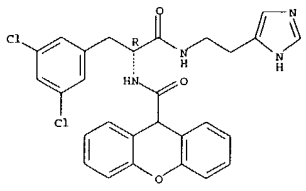
AB Histamines I [X = O, NH; W = CO, CH2; R = nonarom. heterocyclyl, alicyclyl, (un)substituted C7-12 aralkyl; Y = (halo-substituted) aryl; B = H, carbamoyl, amino-C1-3 alkylcarbamoyl], their pharmacol. acceptable salts, or esters are prepared Amidation of D-2-hydroxy-3-(1-naphthyl)propionic acid with N(im)-tritylhistamine, esterification of the resulting amide with 1-naphthalenecarboxylic acid, and detritylation of the product gave I (X = O, W = CO, R = Y = 1-naphthyl, B = H), which inhibited geranylgeranyl transferase I of Candida albicans with IC50 of 11 nM.

IT **285980-03-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of histamines as inhibitors of protein geranylgeranyl transferase I for use of antifungal agents)

RN 285980-03-2 CAPLUS
CN 9H-Xanthene-9-carboxamide, N-[(1R)-1-[(3,5-dichlorophenyl)methyl]-2-[[2-(1H-imidazol-4-yl)ethyl]amino]-2-oxoethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 128 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 129 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

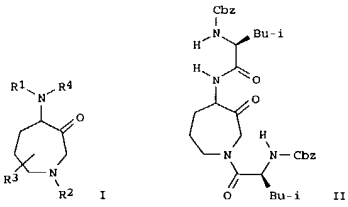
ACCESSION NUMBER: 2000:456887 CAPLUS
DOCUMENT NUMBER: 133:89444
TITLE: Preparation of 4-amino-azepan-3-one protease inhibitors
INVENTOR(S): Marquis, Robert Wells, Jr.; Ru, Yu; Veber, Daniel Frank; Cummings, Maxwell David; Thompson, Scott Kevin; Yamashita, Dennis
PATENT ASSIGNEE(S): Smithkline Beecham Corp., USA
SOURCE: PCT Int. Appl., 273 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038687	A1	20000706	WO 1999-US30730	19991221
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MA, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2356671	AA	20000706	CA 1999-2356671	19991221
BR 9916488	A	20011009	BR 1999-16488	19991221
EP 1158986	A1	20011205	EP 1999-963112	19991221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002533397	T2	20021008	JP 2000-590640	19991221
AU 768565	B2	20031218	AU 2000-19411	19991221
NZ 511710	A	20031219	NZ 1999-511710	19991221
EP 1384713	A1	20040128	EP 2003-76211	19991221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY				
ZA 2001004208	A	20020523	ZA 2001-4208	20010523
US 2003144175	A1	20030731	US 2001-881334	20010614
NO 2001003124	A	20010622	NO 2001-3124	20010622
US 2002147188	A1	20021010	US 2002-74940	20020213
US 2003044399	A1	20030306	US 2002-74639	20020213
US 2003225061	A1	20031204	US 2003-404142	20030401
US 2004002487	A1	20040101	US 2003-404716	20030401

PRIORITY APPLN. INFO.:
US 1998-113636P P 19981223
US 1999-164581P P 19991110
EP 1999-963112 A3 19991221
WO 1999-US30730 W 19991221
US 2000-593845 B2 20000614
US 2000-653815 A1 20000901
US 2001-881334 A1 20010614
US 2002-74940 A1 20020213

OTHER SOURCE(S): MARPAT 133:89444
GI

L4 ANSWER 129 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



I

II

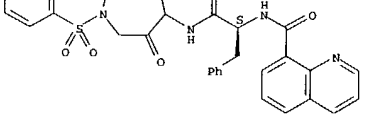
AB The title compds. [I; R1 = COCR13NR11R12, COCR13XR15, COCH2R13; R2 = H, alkyl, cycloalkylalkyl, etc.; R3 = H, alkyl, cycloalkylalkyl, etc.; R4 = H, alkyl, arylalkyl, etc.; R11 = H, alkyl, arylalkyl, etc.; R12 = H, alkyl, cycloalkyl, etc.; R13 = H, alkyl, alkenyl, etc.; R15 = H, alkyl, alkenyl, etc.] which inhibit proteases (no data), including cathepsin K, and are useful for treating diseases of excessive bone loss or cartilage or matrix degradation including osteoporosis, gingival disease including gingivitis and periodontitis, arthritis, more specifically, osteoarthritis and rheumatoid arthritis, Paget's disease, hypercalcemia of malignancy, and metabolic bone disease, were prepared E.g., a multi-step synthesis of compound II was given. Compds. I are effective at 0.4-400 mg/kg/day.

IT **281217-12-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 4-amino-azepan-3-one protease inhibitors)

RN 281217-12-7 CAPLUS

CN 8-Quinolinecarboxamide, N-[(1S)-2-[[hexahydro-3-oxo-1-(2-pyridinylsulfonyl)-1H-azepin-4-yl]amino]-2-oxo-1-(phenylmethyl)ethyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 130 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:452347 CAPLUS
DOCUMENT NUMBER: 133:89798
TITLE: Preparation of peptidyl boronic ester and acid compounds as proteasome inhibitors
INVENTOR(S): Adams, Julian; Ma, Yu-Ting; Stein, Ross; Baevsky, Matthew; Grenier, Louis; Plamondon, Louis
PATENT ASSIGNEE(S): Leukosite, Inc., USA
SOURCE: U.S., 38 pp., Cont.-in-part of U.S. Ser. No. 330,525, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

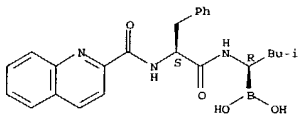
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6083903	A	20000704	US 1995-442581	19950516
CA 2203936	AA	19960509	CA 1995-2203936	19951027
WO 9613266	A1	19960509	WO 1995-US14117	19951027
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9641398	A1	19960523	AU 1996-41398	19951027
AU 710564	B2	19990923		
ZA 9509119	A	19960527	ZA 1995-9119	19951027
EP 788360	A1	19970813	EP 1995-939670	19951027
EP 788360	B1	20030528		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1168633	A	19971224	CN 1995-196590	19951027
US 5780454	A	19980714	US 1995-549318	19951027
JP 10510245	T2	19981006	JP 1995-514834	19951027
NZ 337211	A	20001222	NZ 1995-337211	19951027
IL 115790	A1	20021201	IL 1995-115790	19951027
EP 1312609	A1	20030521	EP 2003-4280	19951027
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
AT 241631	E	20030615	AT 1995-939670	19951027
FI 9701746	A	19970606	FI 1997-1746	19970423
NO 9701929	A	19970612	NO 1997-1929	19970425
US 6066730	A	20000523	US 1998-85404	19980526
US 6297217	B1	20011002	US 2000-490511	20000125
US 6465433	B1	20021015	US 2001-953540	20010914
US 2002173488	A1	20021121	US 2002-100295	20020318
US 6548668	B2	20030415		
US 6617317	B1	20030909	US 2002-125997	20020419
US 2003199561	A1	20031023	US 2003-392165	20030319

PRIORITY APPLN. INFO.:
US 1994-330525 B2 19941028
US 1995-442581 A 19950516
EP 1995-939670 A3 19951027
NZ 1995-296717 A1 19951027
US 1995-549318 A3 19951027
WO 1995-US14117 W 19951027
US 1998-85404 A3 19980526
US 2000-490511 A1 20000125
US 2001-953540 A1 20010914
US 2002-100295 A1 20020318

L4 ANSWER 130 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
US 2002-125997 A1 20020419

OTHER SOURCE(S): MARPAT 133:89798
AB Peptidyl boronic acid and ester compds. P-NRCHR2-X2-CHR3BZ1Z2 [P = 2- or 8-quinolinyl-, 2-quinoxalinyl-, 2- or 3-pyridyl-, piperazinyl-, 3-furanyl-, or 3-pyrrolylcarbonyl, or -sulfonyl, or morpholinylcarbonyl; X2 = CONH, CH2NH, CH(OH)CH2, CH(OH)CH(OH), CH(OH)CH2NH, CH:CH, COCH2, SO2NH, SO2CH2, or CH(OH)CH2CONH; R = H or alkyl; R2, R3 = H, alkyl, cycloalkyl, aryl, heterocyclyl, CH2-R5 (R5 = aryl, aralkyl, alkaryl, cycloalkyl, heterocyclyl) or alkyl-chalcogen; Z1, Z2 = alkyl, hydroxy, alkoxy, aryloxy, or together form a dihydroxy compound] were prepared as proteasome inhibitors. Thus, coupling of (1S,2S,3R,5S)-pinanediol leucine boronate trifluoroacetate salt with N-Boc-β-(1-naphthyl)-L-alanine, followed by deprotection, acylation with 4-morpholinylcarbonyl chloride and cleavage of the pinanediol moiety afforded N-(4-morpholine)carbonyl-β-(1-naphthyl)-L-alanine-L-leucine boronic acid [MG-273], which inhibited 20S proteasome with Ki = 0.18 nM.
IT **179324-53-9P**, MG 314
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptidyl boronic ester and acid compds. as proteasome inhibitors)
RN 179324-53-9 CAPLUS
CN Boronic acid, [(1R)-3-methyl-1-[[(2S)-1-oxo-3-phenyl-2-[(2-quinolinylcarbonyl)amino]propyl]amino]butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

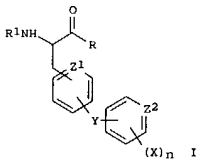


REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 131 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:441762 CAPLUS
DOCUMENT NUMBER: 133:74323
TITLE: Preparation of N-acylphenylalanine derivatives and analogs as inhibitors of α4β1 mediated cell adhesion
INVENTOR(S): Teegarden, Bradley R.; Jayakumar, Honnappa; Matsuki, Kenji; Chrusciel, Robert A.; Fisher, Jed F.; Tanis, Steven P.; Thomas, Edward W.; Blinn, James R.
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan; Pharmacia & Upjohn Company
SOURCE: PCT Int. Appl., 215 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037429	A2	20000629	WO 1999-US30665	19991220
WO 2000037429	A3	20030522		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1144365	A2	20011017	EP 1999-966584	19991220
EP 1144365	A3	20030709		
EP 1144365	B1	20040317		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2003524614	T2	20030819	JP 2000-589501	19991220

PRIORITY APPLN. INFO.: US 1998-113501P P 19981222
WO 1999-US30665 W 19991220
OTHER SOURCE(S): MARPAT 133:74323
GI

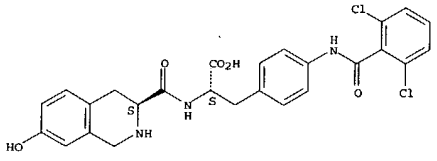


I

L4 ANSWER 131 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

AB Title compds. I [X = halo, CF3, NO2, OH, alkoxy, NH2, alkyl; n = 1-3; Z1, Z2 = CH or N; Y = OCH2 or NHCO; R = OH or alkoxy; R1 = acyl group] or their pharmaceutically acceptable salts were prepared as inhibitors of α4β1 mediated adhesion to either the vascular cell adhesion mol. (VCAM-1) or the CS-1 domain of fibronectin and are useful in the treatment of inflammatory diseases. Approx. 200 invention compds. and their intermediates were prepared by various coupling methods and purified by chromatog. on silica gel. Thus, 4-[(2,6-dichlorobenzoyl)amino]-N-[[(3S)-7-hydroxy-1,2,3,4-tetrahydro-3-isoquinolyl]carbonyl]-L-phenylalanine was prepared by deprotection of resin-bound N-(tert-butoxycarbonyl)-4-[(2,6-dichlorobenzoyl)amino]-L-phenylalanine with 50% TFA/CH2Cl2, followed by treatment with (3S)-2-(tert-butoxycarbonyl)-7-hydroxy-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid, deprotection, and hydrolysis with 2N LiOH. In vitro cell adhesion inhibitory and/or modulatory activities are reported for > 100 invention compds. tested in Jurkat CS-1 and/or Jurkat endothelial cell (EC) adhesion inhibition assays. Ten compds. showed IC50 values ≤ 0.8 μM in both assays.
IT **279239-07-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-acylphenylalanine derivs. and analogs as inhibitors of α4β1 mediated cell adhesion)
RN 279239-07-5 CAPLUS
CN L-Phenylalanine, 4-[(2,6-dichlorobenzoyl)amino]-N-[[(3S)-1,2,3,4-tetrahydro-7-hydroxy-3-isoquinolinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

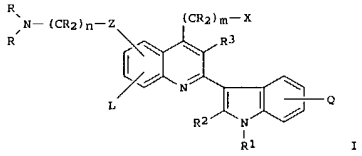


L4 ANSWER 132 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:401813 CAPLUS
DOCUMENT NUMBER: 133:43453
TITLE: Preparation of 2-(3-indolyl)quinolines as antibacterial agents
INVENTOR(S): Cuny, Gregory D.; Hauske, James R.; Heefner, Donald L.; Hoemann, Michael Z.; Kumaravel, Gnanasambandam; Melikian-Badalian, Anita; Rossi, Richard F.; Xie, Roger L.
PATENT ASSIGNEE(S): Sepracor, Inc., USA
SOURCE: PCT Int. Appl., 155 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

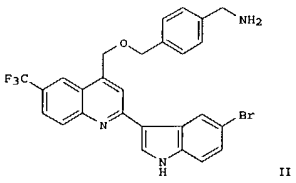
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000034265	A2	20000615	WO 1999-US28744	19991203
WO 2000034265	A3	20021003		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6103905	A	20000815	US 1998-213385	19981211

PRIORITY APPLN. INFO.: US 1998-213385 A 19981211
US 1997-878781 B2 19970619
US 1998-45051 A2 19980319
US 1998-99640 A2 19980618
OTHER SOURCE(S): MARPAT 133:43453
GI

L4 ANSWER 132 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



I



II

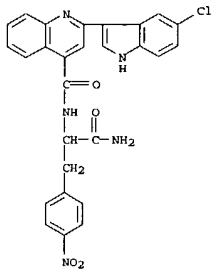
AB The title compds. (I) [wherein L and Q = independently a hydrophobic group or is absent; X = heterocyclyl, (form)amidinyl, guanidinyl, CN, C(S)NR2, N(R)C(S)R, OR, SR, NR2, or PR2; Z = C.tplbond.C, CH:CH, or CH2CH2; R = independently H, (hetero)alkyl, (hetero)aryl, acyl, sulfonyl, etc.; R1 = H, alkyl, aryl, p-toluenesulfonyl, phthalimidoalkyl, or aminoalkyl; R2 and R3 = independently H, alkyl, or acyl] were prepared by standard synthetic and solid phase combinatorial methods. For example, II was synthesized in a 3-step sequence involving: (1) reduction of 2-[5-bromo-1-(tert-butoxycarbonyl)indol-3-yl]-6-(trifluoromethyl)-4-quinolinecarboxylic acid to the alc. with LiAlH4 (44%), (2) addition of 4-iodo-N-(tert-butoxycarbonyl)benzylamine (preparation given) to the alc. (82%), and (3) indolyl and amine deprotection using TFA (78%). Nearly two-thirds of the 534 indolylquinolines tested in assays against cultures of methicillin-resistant Staphylococcus aureau (MRSA), ciprofloxacin-resistant Staphylococcus aureus (CRSA), vancomycin-resistant Enterococcus spp.(VRE), and/or penicillin-resistant Pseudomonas (PRP) had in vitro min. inhibitory concns. (MICs) ≤ 10 μM. For 12 of the 15 compds. tested in vivo for toxicity, all mice were surviving 7 days after administration of 40 mg/kg doses.

IT **275357-08-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-(3-indolyl)quinolines as antibacterial agents)

RN 275357-08-9 CAPLUS

CN 4-Quinolinecarboxamide, N-[2-amino-1-[(4-nitrophenyl)methyl]-2-oxoethyl]-2-(5-chloro-1H-indol-3-yl)- (9CI) (CA INDEX NAME)

L4 ANSWER 132 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 133 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

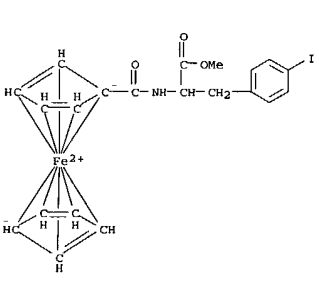
ACCESSION NUMBER: 2000:358667 CAPLUS
DOCUMENT NUMBER: 133:177433
TITLE: P-C bond formation: synthesis of phosphino amino acids by palladium-catalyzed cross-coupling
AUTHOR(S): Kraatz, Heinz-Bernhard; Pletsch, Andreas
CORPORATE SOURCE: Department of Chemistry, University of Saskatchewan, Saskatoon, SK, S7N 5C9, Can.
SOURCE: Tetrahedron: Asymmetry (2000), 11(7), 1617-1621
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:177433

AB (4-Diethylphosphinyl)- and (4-diphenylphosphinyl) derivs. of D- and L-phenylalanine were synthesized using a Pd-catalyzed cross-coupling giving the desired products in very high yields and without racemization.

IT **288263-21-8**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of phosphino amino acids by palladium-catalyzed cross-coupling)

RN 288263-21-8 CAPLUS

CN Ferrocene, [[[(1S)-1-[(4-iodophenyl)methyl]-2-methoxy-2-oxoethyl]amino]carbonyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 134 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:351382 CAPLUS
DOCUMENT NUMBER: 132:330369
TITLE: Treatment of tumors by administration of growth hormone releasing compounds and their antagonists
INVENTOR(S): Muccioli, Giampiero; Papotti, Mauro; Ghigo, Ezio; Deghenghi, Romano
PATENT ASSIGNEE(S): Asta Medica Aktiengesellschaft, Germany
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000029011	A1	20000525	WO 1999-EP8662	19991111
W: AU, BG, BR, BY, CA, CN, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6124263	A	20000926	US 1998-192406	19981116
BR 9915390	A	20010807	BR 1999-15390	19991111
EP 1131083	A1	20010912	EP 1999-955974	19991111
EP 1131083	B1	20040121		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002529512	T2	20020910	JP 2000-582057	19991111
NZ 511280	A	20021025	NZ 1999-511280	19991111
AU 768516	B2	20031218	AU 2000-12706	19991111
ZA 2001003182	A	20010907	ZA 2001-3182	20010419
NO 2001002367	A	20010709	NO 2001-2367	20010514
BG 105572	A	20020131	BG 2001-105572	20010607

PRIORITY APPLN. INFO.: US 1998-192406 A 19981116
AU 1999-43717 A3 19990528
WO 1999-EP8662 W 19991111

OTHER SOURCE(S): MARPAT 132:330369

AB A method for treating a tumor in a mammal by administering a growth hormone releasing compound or an antagonist thereof in an amount effective to reduce or inhibit proliferation of tumorigenic cells in the mammal. In particular, the tumors to be treated include lung, mammary, thyroid or pancreas tumors. The preferred compds. are certain peptides that contain Me tryptophan and lysine units.

IT **268545-46-6**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of tumors by administration of growth hormone releasing compds. and antagonists)

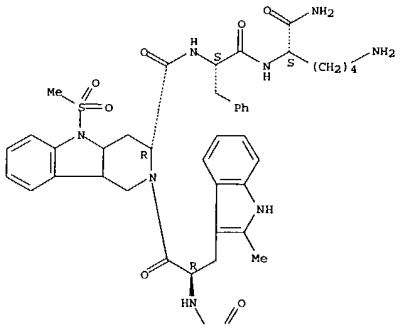
RN 268545-46-6 CAPLUS

CN L-Lysinamide, 2-methyl-N-[(2S)-4-methyl-1-oxo-2-[(5S)-6-oxo-1,7-diazaspiro[4.4]non-7-yl]pentyl]-D-tryptophyl-(3R)-2,3,4,4a,5,9b-hexahydro-5-(methylsulfonyl)-1H-pyrido[4,3-b]indole-3-carbonyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

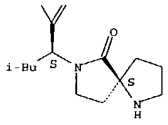
Absolute stereochemistry.

L4 ANSWER 134 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

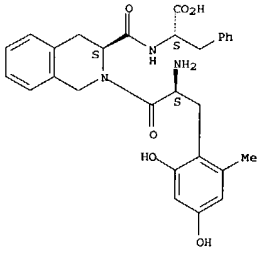


PAGE 2-A



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 135 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 135 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:288696 CAPLUS
DOCUMENT NUMBER: 133:12871
TITLE: Opioid peptide analogs containing 2'-hydroxy,6'-methyltyrosine in place of Tyr1 display greatly enhanced δ antagonist potency but unchanged μ agonist potency
AUTHOR(S): Berezowska, Irena; Lemieux, Carole; Nguyen, Thi M.-D.; Chung, Nga N.; Schiller, Peter W.
CORPORATE SOURCE: Clinical Research Institute of Montreal, Montreal, QC, H2W 1R7, Can.
SOURCE: Peptides 1998, Proceedings of the European Peptide Symposium, 25th, Budapest, Aug. 30-Sept. 4, 1998 (1999), Meeting Date 1998, 718-719. Editor(s): Bajusz, Sandor; Hudecz, Ferenc. Akademiai Kiado: Budapest, Hung.
CODEN: 68WKAY
DOCUMENT TYPE: Conference
LANGUAGE: English

AB The authors report the syntheses and in vitro opioid activity profiles of the Hmt1-analogs of the δ antagonists TIP (H-Tyr-Tic-Phe-OH) and TIPP (H-Tyr-Tic-Phe-Phe-OH) and of the μ agonists TAPP (H-Tyr-D-Ala-Phe-Phe-NH2) and DALDA (H-Tyr-D-Arg-Phe-Lys-NH2). In vitro opioid activities of the compds. were determined in the μ-receptor-representative guinea pig ileum assay and in the δ receptor-representative mouse vas deferens (MVD) assay, and their μ and δ receptor affinities were measured in binding assays based on displacement of [3H]DAMGO and [3H]DSLET, resp., from rat brain membrane binding sites. The tripeptide H-Hmt-Tic-Phe-OH was an about 15 times more potent δ antagonist against the δ agonist DPDPE than its parent TIP, showing δ antagonist potency (MVD) and δ receptor binding affinity in the subnanomolar range. Furthermore, this compound showed greatly improved δ receptor selectivity as compared to TIP. The Hmt1-analog of the tetrapeptide TIPP, H-Hmt-Tic-Phe-Phe-OH, displayed very high δ antagonist potency in the MVD assay, comparable to that of H-Dmt-Tic-Phe-Phe-OH. In the binding assays, it showed slightly higher δ receptor affinity than H-Dmt-Tic-Phe-Phe-OH and 20-fold higher δ selectivity. Thus, [Hmt1]TIPP ranks among the most potent and most specific δ opioid antagonists reported to date. Substitution of Hmt for Tyr1 in the μ agonist peptides TAPP and DALDA resulted in μ-agonist potencies comparable to those of their resp. parent peptides.. In conclusion, replacement of Tyr1 in opioid peptides with Hmt produced a potency increase in the case of the δ antagonists but not in the case of the μ agonists.

IT **271795-36-9**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(opioid peptide analogs δ antagonist and μ agonist activity in relation to structure)

RN 271795-36-9 CAPLUS
CN L-Phenylalanine, 2-hydroxy-6-methyl-L-tyrosyl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 136 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

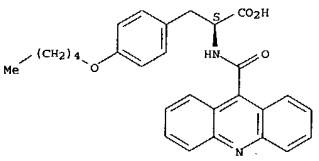
ACCESSION NUMBER: 2000:269112 CAPLUS
DOCUMENT NUMBER: 133:37726
TITLE: N-acyl phenylalanine analogues as potent small molecule VLA-4 antagonists
AUTHOR(S): Chen, Li; Tilley, Jefferson W.; Huang, Tai-Nan; Miklowski, Dorota; Trilles, Richard; Guthrie, Robert W.; Luk, Kin; Hanglow, Angela; Rowan, Karen; Schwinge, Virginia; Wolitzky, Barry
CORPORATE SOURCE: Roche Research Center, Hoffmann-La Roche, Inc., Nutley, NJ, 07110, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2000), 10(8), 725-727
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have identified a series of low mol. weight (Mr <500) N-acylphenylalanines that are effective inhibitors of the VCAM-VLA-4 interaction. Investigation of the SAR of the N-acyl moiety led to the identification of N-benzylpyroglutamyl derivs. as being particularly potent.

IT **275802-12-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(N-acyl phenylalanine analogs as VLA-4 antagonists)

RN 275802-12-5 CAPLUS
CN L-Tyrosine, N-(9-acridinylcarbonyl)-O-pentyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

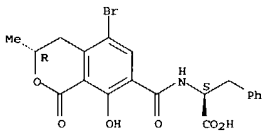
L4 ANSWER 137 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:236481 CAPLUS
DOCUMENT NUMBER: 133:28301
TITLE: Influence of Halogen Salts on the Production of the Ochratoxins by Aspergillus ochraceus Wilh.
AUTHOR(S): Stander, Maria A.; Steyn, Pieter S.; Luebben, Annelie; Miljkovic, Ana; Mantle, Peter G.; Marais, Gert J.
CORPORATE SOURCE: School of Chemistry and Biochemistry, University of Potchefstroom, Potchefstroom, 2520, S. Afr.
SOURCE: Journal of Agricultural and Food Chemistry (2000), 48(5), 1865-1871
CODEN: JAFCAU; ISSN: 0021-8561
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The first report of the biol. production of bromo ochratoxin B by Aspergillus ochraceus Wilh. is presented as well as a study of the influence of potassium bromide, potassium iodide, potassium fluoride, and potassium chloride on the production of ochratoxin A and ochratoxin B. Potassium fluoride and potassium iodide inhibited the growth of the fungus, whereas potassium chloride substantially stimulated the production of ochratoxin A in shaken solid substrate fermentation on whole wheat or shredded wheat, generally giving a high yield of ochratoxins. Increasing levels of potassium bromide led to a decline in ochratoxin A production and an increase in bromo-ochratoxin B, ochratoxin B, and 4-hydroxy ochratoxin B. Nevertheless, A. ochraceus was much less versatile in the bromo analogs than other fungi, which produce metabolites containing chlorine. Anal. included aminopropyl solid-phase extraction column cleanup followed by quant. anal. on reversed-phase HPLC using fluorescence detection and employing N-(5-chloro-2-hydroxybenzoyl)phenylalanine as an internal standard

IT **255042-26-3P**
RL: PRP (Properties); PUR (Purification or recovery); PREP (Preparation) (influence of potassium halides on production of ochratoxins by Aspergillus ochraceus)

RN 255042-26-3 CAPLUS
CN L-Phenylalanine, N-[[(3R)-5-bromo-3,4-dihydro-8-hydroxy-3-methyl-1-oxo-1H-2-benzopyran-7-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 138 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:144899 CAPLUS
DOCUMENT NUMBER: 132:189658
TITLE: Amino acid derivative and peptide anti-cancer compounds and methods
INVENTOR(S): Stewart, John M.; Chan, Daniel C. F.; Gera, Lojos; York, Eunice; Bunn, Paul
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000011022	A1	20000302	WO 1999-US19381	19990820
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6388054	B1	20020514	US 1999-378019	19990819
AU 2000015959	A1	20000314	AU 2000-15959	19990820
US 2002183252	A1	20021205	US 2001-35662	20011228
PRIORITY APPLN. INFO.:			US 1998-97210P P	19980820
			US 1999-141169P P	19990625
			US 1999-378019 A	19990819
			WO 1999-US19381 W	19990820

OTHER SOURCE(S): MARPAT 132:189658

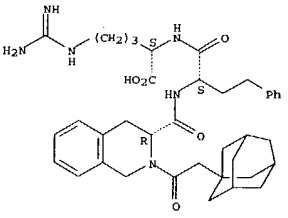
AB The invention provides amino acid derivative and peptidic compds. useful to inhibit tumor growth and to induce apoptosis. In general, the anti-cancer agents (ACA) are described by the formula [ACA]n-X [X = linker group with 2-5 functional groups or is absent; n = 1; ACA as described in the invention (Markush included)].

IT **259883-84-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptide and non-peptide anti-cancer compds. and methods)

RN 259883-84-6 CAPLUS
CN L-Arginine, N2-[(2S)-1-oxo-4-phenyl-2-[[[(3R)-1,2,3,4-tetrahydro-2-(tricyclo[3.3.1.13,7]dec-1-ylacetyl)-3-isoquinolinyl]carbonyl]amino]butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 138 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 139 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:84777 CAPLUS
DOCUMENT NUMBER: 132:137288
TITLE: Preparation of isoquinolinylguanidines as urokinase inhibitors
INVENTOR(S): Barber, Christopher Gordon; Dickinson, Roger Peter; Fish, Paul Vincent
PATENT ASSIGNEE(S): Pfizer Inc., USA; Pfizer Limited
SOURCE: PCT Int. Appl., 222 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000005214	A2	20000203	WO 1999-IB1289	19990715
WO 2000005214	A3	20010531		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2337247	AA	20000203	CA 1999-2337247	19990715
AU 9945289	A1	20000214	AU 1999-45289	19990715
AU 745545	B2	20020321		
EP 1077945	A1	20010228	EP 1999-928177	19990715
EP 1077945	B1	20030108		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9912374	A	20010417	BR 1999-12374	19990715
EE 200100049	A	20020617	EE 2001-49	19990715
JP 2002521367	T2	20020716	JP 2000-561170	19990715
AT 230730	E	20030115	AT 1999-928177	19990715
PT 1077945	T	20030331	PT 1999-99928177	19990715
ES 2189434	T3	20030701	ES 1999-928177	19990715
TW 530049	B	20030501	TW 1999-88112548	19990723
ZA 2001000230	A	20020301	ZA 2001-230	20010109
NO 2001000400	A	20010326	NO 2001-400	20010123
HR 2001000059	A1	20020228	HR 2001-59	20010123
BG 105252	A	20011231	BG 2001-105252	20010214
PRIORITY APPLN. INFO.:			GB 1998-16228 A	19980724
			GB 1999-8829 A	19990416
			WO 1999-IB1289 W	19990715

OTHER SOURCE(S): MARPAT 132:137288

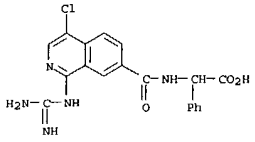
AB R3Z1R2Z2ZR [I; R = N:C(NH2)2 or NHC(:NH)NH2; R2 = H, alkyl, (hetero)aryl, etc.; R3 = CO2R7, CH2OH, CONR8R9, CH2NR8R9; R7 = H or alkyl; R8,R9 = H, (hydroxy)alkyl, etc.; NR8R9 = heterocyclyl; Z = (4-chloro) isoquinoline-7,1-diyl; Z1 = (cyclo)alkylene, heterocyclylene, arylene, etc.; Z1NR2 = azetidine-, pyrrolidine-, or (homo)piperidinediyl; Z2 = CO, CH2, SO2] were prepared Thus, 2-(H2N)C6H4CO2CMe3 was condensed with 7-bromo-1,4-dichloroisoquinoline (preparation each given) and SOCl2 and the product iminated by (H2N)2C:NH to give, after saponification, 2-(HO2C)C6H4NHSO2ZN:C(NH2)2.HCl (R = 4-chloroisoquinoline-7,1-diyl). Data for biol. activity of I were given.

IT **256476-58-1P**

L4 ANSWER 139 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of isoquinolinylguanidines as urokinase inhibitors)
RN 256476-58-1 CAPLUS
CN Benzeneacetic acid, α-[[[1-[(aminoiminomethyl)amino]-4-chloro-7-isoquinolinyl]carbonyl]amino]-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 256476-57-0
CMF C19 H16 Cl N5 O3

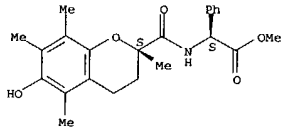


CM 2

CRN 76-05-1
CMF C2 H F3 O2

L4 ANSWER 140 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:814 CAPLUS
DOCUMENT NUMBER: 132:207466
TITLE: Phenylglycine Methyl Ester, a Useful Tool for Absolute Configuration Determination of Various Chiral Carboxylic Acids
AUTHOR(S): Yabuuchi, Tetsuya; Kusumi, Takenori
CORPORATE SOURCE: Faculty of Pharmaceutical Sciences, Tokushima University, Tokushima, 770-8505, Japan
SOURCE: Journal of Organic Chemistry (2000), 65(2), 397-404
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A new chiral anisotropic reagent, phenylglycine Me ester (PGME), developed for the elucidation of the absolute configuration of chiral α,α-disubstituted acetic acids, has turned out to be applicable to other substituted carboxylic acids, such as chiral α-hydroxy-, α-alkoxy-, and α-acyloxy α,α-disubstituted acetic acids, as well as to chiral β,β-disubstituted propionic acids. Because a carboxylic moiety is convertible from other functional groups, e.g., ozonolysis of an olefin and oxidative cleavage of a glycol, the present findings can expand the utility of the PGME method to the absolute configuration determination of various types of organic compds., even those which initially lack oxygen functions. Several examples of the combination of chemical reactions and the PGME method are described.
IT **259877-12-8P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(determination of absolute configuration of chiral carboxylic acids using phenylglycine Me ester as anisotropic reagent)
RN 259877-12-8 CAPLUS
CN Benzeneacetic acid, α-[[[(2S)-3,4-dihydro-6-hydroxy-2,5,7,8-tetramethyl-2H-1-benzopyran-2-yl]carbonyl]amino]-, methyl ester, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



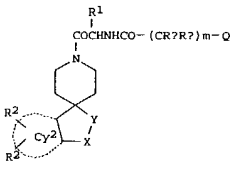
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 141 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:795654 CAPLUS
DOCUMENT NUMBER: 132:22957
TITLE: Preparation of spiropiperidine derivatives as melanocortin receptor agonists
INVENTOR(S): Nargund, Ravi P.; Ye, Zhixiong; Palucki, Brenda L.; Bakshi, Raman K.; Patchett, Arthur A.; Van Der Ploeg, Leonardus H. T.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9964002	A1	19991216	WO 1999-US13252	19990610
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2334551	AA	19991216	CA 1999-2334551	19990610
AU 9946801	A1	19991230	AU 1999-46801	19990610
AU 742425	B2	20020103		
EP 1085869	A1	20010328	EP 1999-930220	19990610
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO				
US 6294534	B1	20010925	US 1999-329814	19990610
JP 2002517444	T2	20020618	JP 2000-553071	19990610
US 2001029259	A1	20011011	US 2001-781373	20010212
US 6410548	B2	20020625		

PRIORITY APPLN. INFO.: US 1998-88908P P 19980611
GB 1998-17179 A 19980806
US 1999-123260P P 19990308
US 1999-329814 A3 19990610
WO 1999-US13252 W 19990610
OTHER SOURCE(S): MARPAT 132:22957
GI

L4 ANSWER 141 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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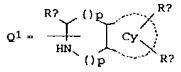
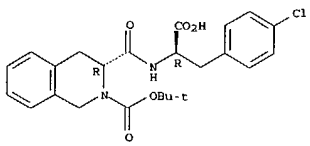


AB Certain novel spiropiperidine compds. I [Cy2 = six-membered aromatic ring containing 0 or 1 N; X = O, CH2, etc.; Q = Q1; Y = CO, SO2, etc; R1, Rb = H, C1-8 alkyl, etc.; R2 = H or halo; Rc = Rb, halo, ORb, NHSO2Rb, N(Rb)2, SO2Rb, CF3, OCF3; Cy = aryl, 5 or 6 membered heteroaryl, 5 or 6 membered heterocyclyl, 5 or 6 membered carbocyclyl; m, p, q independently = 0, 1, or 2] are agonists of melanocortin receptors (no data) and are useful for the treatment, control or prevention of diseases and disorders responsive to the activation of melanocortin receptors. The compds. of the present invention are therefore useful for treatment of diseases and disorders such as obesity, diabetes, sexual dysfunction including erectile dysfunction and female sexual dysfunction.
IT **252008-71-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of spiropiperidine derivs. as melanocortin receptor agonists)
RN 252008-71-2 CAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3-[[[(1R)-1-carboxy-2-(4-chlorophenyl)ethyl]amino]carbonyl]-3,4-dihydro-, 2-(1,1-dimethylethyl) ester, (3R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 141 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

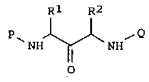
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 142 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:753019 CAPLUS
DOCUMENT NUMBER: 132:12506
TITLE: Preparation of peptides for treating diseases of excessive bone loss or cartilage or matrix degradation as cysteine protease inhibitors
INVENTOR(S): Bondinell, William Edward; Desjarlais, Renee Louise; Veber, Daniel Frank; Yamashita, Dennis Shinji
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 128 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9959526	A2	19991125	WO 1999-US11266	19990520
WO 9959526	A3	20000120		
W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CZ, EE, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2332531	AA	19991125	CA 1999-2332531	19990520
EP 1067894	A2	20010117	EP 1999-924421	19990520
R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
JP 2002515411	T2	20020528	JP 2000-549192	19990520
US 6518267	B1	20030211	US 2000-700828	20001121

PRIORITY APPLN. INFO.: US 1998-86557P P 19980521
WO 1999-US11266 W 19990520
OTHER SOURCE(S): MARPAT 132:12506
GI



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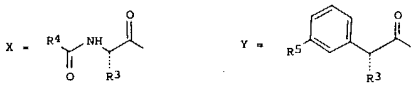


AB The present invention provides peptides bis-aminomethyl carbonyl protease

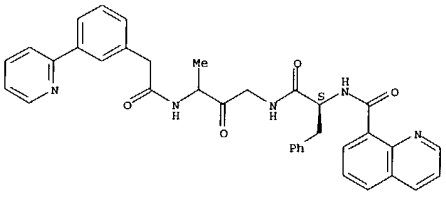
L4 ANSWER 142 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

inhibitors I (R1, R2 = alkyl; P = X, Y; R3 selected from the group consisting of: CH2CH(CH3)2, CH2CH2CH3, CH2CH=CH2, or CH2Ph; R4 is selected from the group consisting of alkyl; N-piperazine; N-tetrahydroisoquinoline; substituted alkyl, Ph, benzofuran, benzothiazole; quinoline; naphthyl; and benzoxazole; R5 = Ph and Ph substituted with alkyl, N-piperidine, benzofuran; pyridine; Q = arylacyl) and pharmaceutically acceptable salts, hydrates and solvates thereof which inhibit proteases, including cathepsin K, pharmaceutical compns. of such compds., and methods for treating diseases of excessive bone loss or cartilage or matrix degrdn., including osteoporosis; gingival disease including gingivitis and periodontitis; arthritis, more specifically, osteoarthritis and rheumatoid arthritis; Paget's disease; hypercalcemia of malignancy; and metabolic bone disease, comprising inhibiting said bone loss or excessive cartilage or matrix degrdn. by administering to a patient in need thereof a compd. of the present invention. Thus, (S)-3N-(N-(thianaphthenyl-2-carbonyl)-leucinyl)-amino-1N-(3-{2-(1-oxo)-pyridyl}phenylacetyl)-amino-butan-2-one was prepd. for treating diseases of excessive bone loss or cartilage or matrix degrdn. as cysteine protease inhibitor. Detn. of cathepsin K proteolytic catalytic activity of these compds. are reported.

IT **251458-61-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptides for treating diseases of excessive bone loss or cartilage or matrix degradation as cysteine protease inhibitors)

RN 251458-61-4 CAPLUS
CN 8-Quinolinecarboxamide, N-[(1S)-2-oxo-2-[[2-oxo-3-[[[3-(2-pyridinyl)phenyl]acetyl]amino]butyl]amino]-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 143 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

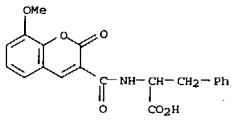
ACCESSION NUMBER: 1999:750286 CAPLUS
DOCUMENT NUMBER: 132:137250
TITLE: Preparation and antibacterial activity of sulfonamido derivatives and amides of coumarin compounds
AUTHOR(S): Shah, Sonal; Desai, Devki; Mehta, R. H.
CORPORATE SOURCE: Department of Chemistry, Faculty of Science, M. S. University of Baroda, Vadodara, 390 002, India
SOURCE: Journal of the Indian Chemical Society (1999), 76(10), 507-508
CODEN: JICSAH; ISSN: 0019-4522
PUBLISHER: Indian Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Coumarin sulfonamide derivs. I and II (R = Me, MeO, AcNH, Cl, Br; R1 = H, Br) were prepared by sulfonylation of an aminophenylaminocarbonyl coumarin, and by nucleophilic displacement of a chloromethyl coumarin with o-phenylenedimaine followed by sulfonylation. Coumarin derivs. III (R2 = Me, Me2CH, MeSCH2CH2, HOCH2; X = bond) and their racemic derivs (R2 = H, Me, Me2CH, MeSCH2CH2, PhCH2; X = bond, CH2) were also prepared from a coumarin acid chloride and racemic and L-amino acid derivs. I, II, and III were tested for their antibiotic activity against E. coli, S. aureus, S. typhosa, and S. albus; I and II showed moderate to low activity against the tested bacteria, while the coumarins III showed no activity against any of the bacteria.

IT **256658-76-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antibacterial activity of coumarin sulfonamide and amino acid derivs.)

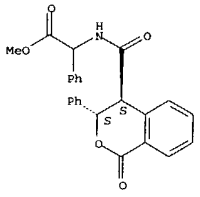
RN 256658-76-1 CAPLUS
CN Phenylalanine, N-[(8-methoxy-2-oxo-2H-1-benzopyran-3-yl)carbonyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

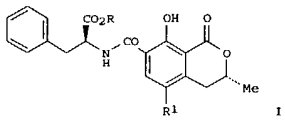
L4 ANSWER 144 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:735984 CAPLUS
DOCUMENT NUMBER: 132:107853
TITLE: Cycloaddition of homophthalic anhydrides with aldehydes and ketones: a route to 3,4-dihydroisocoumarin-4-carboxylic acid derivatives
AUTHOR(S): Yu, Neifang; Poulain, Rebecca; Tartar, Andre; Gesquiere, Jean-Claude
CORPORATE SOURCE: Faculte de Pharmacie, Institut Pasteur and UMR CNRS, Lille, 59006, Fr.
SOURCE: Tetrahedron (1999), 55(48), 13735-13740
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:107853
AB Homophthalic anhydride (1H-2-benzopyran-1,3(4H)-dione) reacts with benzaldehyde, in the presence of boron trifluoride - di-Et ether complex to give the cycloadduct 3-phenyl-3,4-dihydroisocoumarin-4-carboxylic acid in good to excellent yield. Under these conditions, we did not observe the formation of Perkin-type products. The reaction can be extended to a wide variety of aldehydes and to some ketones in synthetically useful yields. Amides can be obtained in good yields after activation of the carboxylic function with DCC at 0°C.
IT **255841-53-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of dihydroisocoumarincatboxamides via cycloaddn. of homophthalic anhydrides with aldehydes or ketones)
RN 255841-53-3 CAPLUS
CN Benzeneacetic acid, α-[[[(3R,4R)-3,4-dihydro-1-oxo-3-phenyl-1H-2-benzopyran-4-yl]carbonyl]amino]-, methyl ester, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

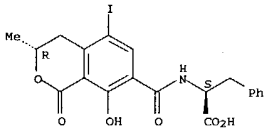
L4 ANSWER 145 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:735231 CAPLUS
DOCUMENT NUMBER: 132:93616
TITLE: The synthesis of bromo- and iodo-ochratoxin B
AUTHOR(S): Steyn, Pieter S.; Payne, Barry E.
CORPORATE SOURCE: School of Chemistry and Biochemistry, Potchefstroom University for CHE, Potchefstroom, 2520, S. Afr.
SOURCE: South African Journal of Chemistry (1999), 52(2/3), 69-70
CODEN: SAJCDG; ISSN: 0379-4350
PUBLISHER: South African Chemical Institute
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 132:93616
GI



I

AB The effective synthesis of 5-bromo- and 5-iodoochratoxin B I (R = H, R1 = Br, iodo) by halogenation of ochratoxin B I (R = R1 = H) with pyridinium hydrobromide perbromide, and iodine and mercury(II) oxide, resp., was reported. 5-Iodoochratoxin B was further converted to 5-iodoochratoxin B Me ester I (R = Me, R1 = iodo) using thionyl chloride and methanol.
IT **255042-27-4P**, 5-Iodoochratoxin B
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(synthesis of bromo- and iodo-ochratoxin B)
RN 255042-27-4 CAPLUS
CN L-Phenylalanine, N-[[(3R)-3,4-dihydro-8-hydroxy-5-iodo-3-methyl-1-oxo-1H-2-benzopyran-7-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



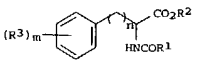
REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 145 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L4 ANSWER 146 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:708602 CAPLUS
DOCUMENT NUMBER: 131:310837
TITLE: Preparation of phenylalanine sulfonamide derivatives and related compounds as CCR-3 receptor antagonists
INVENTOR(S): Dhanak, Dashyant; Widdowson, Katherine L.; White, John R.
PATENT ASSIGNEE(S): Smithkline Beecham Corporation, USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9955330	A1	19991104	WO 1999-US8950	19990427
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2329821	AA	19991104	CA 1999-2329821	19990427
EP 1073434	A1	20010207	EP 1999-921462	19990427
R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
JP 2002512960	T2	20020508	JP 2000-545529	19990427
PRIORITY APPLN. INFO.:			US 1998-83229P P	19980427
			WO 1999-US8950 W	19990427

OTHER SOURCE(S): MARPAT 131:310837
GI

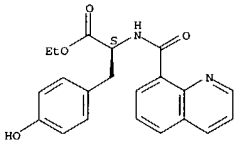


I

AB The title compds. I [R1 = alkyl, aryl, heteroaryl, etc.; R2 = alkyl, benzyl; R3 = OH, alkoxy, NO2, NH2, etc.; m = 1-3; n = 0-3] and EtO2CCHRNHCOPh (R = indolylmethyl, Ph, CH2CH2Ph), CCR-3 receptor antagonists (no data), were prepared E.g., (S)-Et 2-benzoylamino-3-(4-nitrophenyl)propionate was prepared
IT **247580-60-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenylalanine sulfonamide derivs. and related compds. as CCR-3 receptor antagonists)
RN 247580-60-5 CAPLUS
CN L-Tyrosine, N-(8-quinolinylcarbonyl)-, ethyl ester (9CI) (CA INDEX NAME)

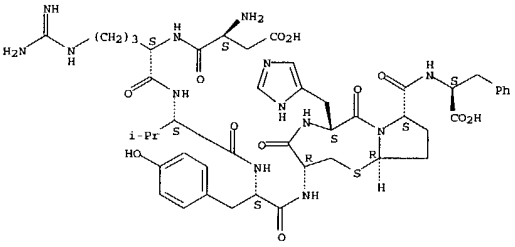
Absolute stereochemistry.

L4 ANSWER 146 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 147 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 66 THERE ARE 66 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 147 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:655304 CAPLUS
DOCUMENT NUMBER: 132:64499
TITLE: Angiotensin II analogs encompassing 5,9- and 5,10-fused thiazabicycloalkane tripeptide mimetics
AUTHOR(S): Johannesson, Petra; Lindeberg, Gunnar; Tong, Weimin; Gogoll, Adolf; Synnergren, Barbro; Nyberg, Fred; Karlen, Anders; Hallberg, Anders
CORPORATE SOURCE: Department of Organic Pharmaceutical Chemistry, Uppsala University, Uppsala, SE-751 23, Swed.
SOURCE: Journal of Medicinal Chemistry (1999), 42(22), 4524-4537
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A simple exptl. procedure on solid phase for the construction of new tripeptidic 5,9- and 5,10-fused thiazabicycloalkane scaffolds that adopt β-turns has been developed. This N terminal-directed bicyclization, relying on masked aldehyde precursors derived from glutamic acid as key building blocks, provides a complement to the related bicyclization previously reported, where an aspartic acid-derived precursor was employed to induce cyclization toward the C-terminal end of the peptide. Thus, the regioselectivity of the bicyclization can be altered simply by varying the chain length of the incorporated aldehyde precursor. Four analogs of the hypertensive octapeptide angiotensin II, comprising the new scaffolds in the 3-5- and 5-7-positions, were synthesized. One of these conformationally constrained angiotensin II analogs exhibited AT1 receptor affinity (Ki = 750 nM). Results from theor. conformational anal. of model compds. of the bicyclic tripeptide mimetics are presented, and they demonstrate that subtle differences in geometry have a strong impact on the affinity to the AT1 receptor.

IT **253277-45-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and biol. activity of angiotensin II analogs containing thiazabicycloalkane tripeptide mimetics)

RN 253277-45-1 CAPLUS
CN L-Phenylalanine, L-α-asparty1-L-arginyl-L-valyl-L-tyrosyl-L-cysteinyl-L-histidyl-(5R)-5-mercapto-L-prolyl-, cyclic (5→7)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 148 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

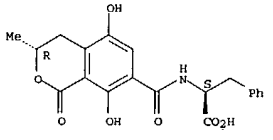
ACCESSION NUMBER: 1999:629552 CAPLUS
DOCUMENT NUMBER: 132:9841
TITLE: Oxidation of Ochratoxin A by an Fe-Porphyrin System: Model for Enzymatic Activation and DNA Cleavage
AUTHOR(S): Gillman, Ivan G.; Clark, T. Nicole; Manderville, Richard A.
CORPORATE SOURCE: Department of Chemistry, Wake Forest University, Winston-Salem, NC, 27109-7486, USA
SOURCE: Chemical Research in Toxicology (1999), 12(11), 1066-1076
CODEN: CRTOEC; ISSN: 0893-228X
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ochratoxin A (OTA) is a fungal toxin that facilitates single-strand DNA cleavage, DNA adduction, and lipid peroxidn. when metabolically activated. To model the enzymic activation of OTA, we have employed the water-soluble iron(III) meso-tetrakis(4-sulfonatophenyl)porphyrin (FeTPPS) oxidation system. In its presence, OTA has been found to facilitate single-strand cleavage of supercoiled plasmid DNA through production of reactive oxygen species (ROS) (i.e., the hydroxyl radical, HO•). The reaction of OTA with the FeTPPS oxidation system also generated three hydroxylated products (chlorine atom still attached), which was taken as evidence for production of the known hydroxylated metabolites of OTA. This result suggested that the FeTPPS system served as a reasonable model for the enzymic activation of OTA. When the reaction of OTA with FeTPPS was carried out in the presence of excess hydrogen peroxide (H2O2) and sodium ascorbate, a hydroquinone species (OTHQ) was detected in which an OH group has replaced the chlorine atom of OTA. The production of OTHQ was dependent on the presence of the reducing agent, sodium ascorbate, which suggested that the oxidation catalyst furnished the quinone derivative OTQ that was subsequently reduced to OTHQ by ascorbate. Utilizing a synthetic sample of OTHQ, the hydroquinone was found to undergo autoxidn. with a t1/2 of 11.1 h at pH 7.4, and to possess a pKa value of 8.03 for the phenolic oxygen ortho to the carbonyl groups. Our findings imply that the hydroquinone (OTHQ) and quinone (OTQ) metabolites of OTA have the ability to cause alkylation/redox damage and have allowed us to propose a viable pathway for oxidative damage by OTA.

IT **205034-32-8P**
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); SPN (Synthetic preparation); BIOL (Biological study); FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process)
(preparation of ochratoxin hydroquinone and oxidation of ochratoxin A by Fe-porphyrin system)

RN 205034-32-8 CAPLUS
CN L-Phenylalanine, N-[[(3R)-3,4-dihydro-5,8-dihydroxy-3-methyl-1-oxo-1H-2-benzopyran-7-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 148 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

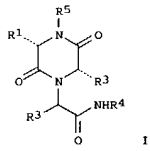
REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 149 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:613947 CAPLUS
DOCUMENT NUMBER: 131:243287
TITLE: Preparation of dioxopiperazinoacetamides as fructose-1,6-bisphosphatase inhibitors
INVENTOR(S): Mjalli, Adnan M. M.; Mason, James Christopher; Arienti, Kristen Lee; Short, Kevin Michael; Kimmich, Rachel Denise Anne; Jones, Todd Kevin
PATENT ASSIGNEE(S): Ontogen Corporation, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9947549	A1	19990923	WO 1999-US5552	19990315
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2289621	AA	19990923	CA 1999-2289621	19990315
AU 9930870	A1	19991011	AU 1999-30870	19990315
US 6107274	A	20000822	US 1999-270121	19990315
EP 1070084	A1	20010124	EP 1999-912505	19990315
R: DE, FR, GB				
JP 2001294586	A2	20011023	JP 2000-386045	19990315

PRIORITY APPLN. INFO.: US 1998-78065P P 19980316
WO 1999-US5552 W 19990315
OTHER SOURCE(S): MARPAT 131:243287
GI



I

AB Title compds. [I; R1 = cycloalkyl or aralkyl; R2 = cycloalkylmethyl or (ar)alkyl; R3 = H, F, alkyl, substituted Ph; R4 = H, alkyl, acyl, substituted Ph; R5 = H; R1R5 = atoms to complete a ring] were prepared Thus, L-R2CH(NH2)CO2Me.HCl (R2 = cyclohexyl), 4-(NC)C6H4CHO, N-Fmoc-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid, and 4-(CNH2CH2C)C6H4OCH2Ph were subjected to Ugi condensation and the product cyclized to give, after deprotection, I [R1R5 = 2-(H2C)C6H4CH2, R2 = cyclohexylmethyl, R3 = 4-(NC)C6H4, R4 = CH2CH2C6H4(OH)-4]. Data for biol.

L4 ANSWER 149 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

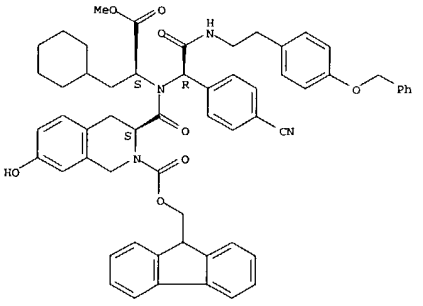
activity of I were given.

IT **244220-68-6P**
RL: BYP (Byproduct); PREP (Preparation)
(preparation of dioxopiperazinoacetamides as fructose-1,6-bisphosphatase inhibitors)

RN 244220-68-6 CAPLUS

CN 2(1H)-Isoquinolinecarboxylic acid, 3-[[[(1R)-1-(4-cyanophenyl)-2-oxo-2-[[2-[4-(phenylmethoxy)phenyl]ethyl]amino]ethyl][(1S)-1-(cyclohexylmethyl)-2-methoxy-2-oxoethyl]amino]carbonyl]-3,4-dihydro-7-hydroxy-, 9H-fluoren-9-ylmethyl ester, (3S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 150 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:583907 CAPLUS
DOCUMENT NUMBER: 131:294930
TITLE: Characterization of spatially addressable libraries: stereoisomer analysis of tetrahydro-β-carbolines as an example
AUTHOR(S): Cheng, Cesar C.; Chu, Yen-Ho
CORPORATE SOURCE: Department of Chemistry, The Ohio State University, Columbus, OH, 43210, USA
SOURCE: Journal of Combinatorial Chemistry (1999), 1(6), 461-466
CODEN: JCCHFF; ISSN: 1520-4766
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

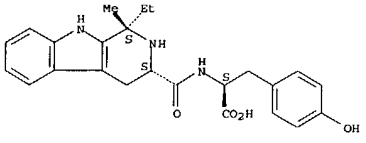
AB Combinatorial chemical approaches have facilitated the process of lead discovery and optimization for new drugs, catalysts, and materials. A successful combinatorial program typically includes high throughput library synthesis, characterization, and screening. One of many challenges in this program is to develop high throughput characterization methods to address issues concerning reaction stereoselectivity and racemization during the library synthesis. Using the core structure of tetrahydro-β-carboline as an example, the authors demonstrate the usefulness of capillary electrophoresis in enantiomeric separation of stereoisomers generated by parallel synthesis and rapid quant. measurement of the isomer ratios, in addition to assessing possible racemization during reactions for its overall potential in library characterization.

IT **246137-76-8P**
RL: ANT (Analyte); PEP (Physical, engineering or chemical process); PRP (Properties); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); PROC (Process)
(characterization of spatially addressable libraries: stereoisomer anal. of tetrahydro-β-carbolines)

RN 246137-76-8 CAPLUS

CN L-Tyrosine, N-[[(1S,3S)-1-ethyl-2,3,4,9-tetrahydro-1-methyl-1H-pyrido[3,4-b]indol-3-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



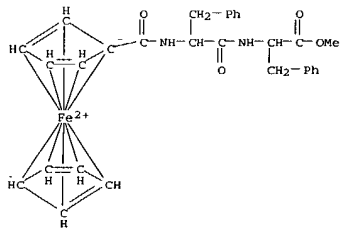
REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 151 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:567712 CAPLUS
DOCUMENT NUMBER: 131:271976
TITLE: Synthesis and electrochemical anion recognition by novel redox-responsive ferrocenoyl dipeptide ester derivatives; 1H NMR anion complexation studies
AUTHOR(S): Gallagher, John F.; Kenny, Peter T. M.; Sheehy, Michael J.
CORPORATE SOURCE: Dublin City University, Dublin, 9, Ire.
SOURCE: Inorganic Chemistry Communications (1999), 2(8), 327-330
CODEN: ICCOFP; ISSN: 1387-7003
PUBLISHER: Elsevier Science S.A.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The synthesis of six N-ferrocenoyl dipeptide ester derivs. FcCOR [Fc = (η5-C5H5)Fe(η5-C5H4); R = Gly-Gly(OMe) (1), Leu-Leu(OEt) (2), Ala-Phe(OEt) (3), Phe-Phe(OMe) (4), Phe-Leu(OBn) (5) and Phe-Ser(OEt) (6)] is described. Derivs. 1-3 were prepared by coupling reactions of FcCO2H with the free N-terminal dipeptide esters. The electrochem. anion sensing behavior (using a Pt microdisk working electrode) and 1H NMR anion coordination studies of these novel pendant N-ferrocenoyl dipeptide ester derivs. with a range of anions are reported. Best results were observed with 1, which sensed halides and dihydrogen phosphate guest anions with marked selectivity, the trend being H2PO4- » Cl- > Br- » HSO4-.

IT **245123-57-3P**
RL: PEP (Physical, engineering or chemical process); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(preparation and complexation of anions by pendant N-ferrocenoyl dipeptide ester derivs.)

RN 245123-57-3 CAPLUS
CN L-Phenylalanine, N-(ferrocenylcarbonyl)-L-phenylalanyl-, methyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

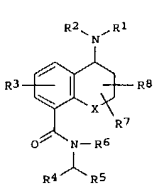
L4 ANSWER 151 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L4 ANSWER 152 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:529142 CAPLUS
DOCUMENT NUMBER: 131:170268
TITLE: Condensed heterocyclic system derivatives, namely 4-amino(thio)chroman-8-carboxamides, useful as farnesyl transferase inhibitors, and their preparation and pharmaceutical compositions
INVENTOR(S): Baudoin, Bernard; Clerc, Francois; Dereu, Norbert; El-Ahmad, Youssef; Hardy, Jean-Claude; Jimonet, Patrick; Le Brun, Alain
PATENT ASSIGNEE(S): Rhone-Poulenc Rorer S.A., Fr.
SOURCE: PCT Int. Appl., 228 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

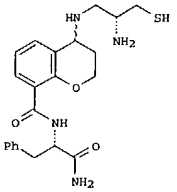
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9941248	A1	19990819	WO 1999-FR298	19990211
W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2774987	A1	19990820	FR 1998-1762	19980213
FR 2774987	B1	20000317		
ZA 9901073	A	19990810	ZA 1999-1073	19990210
CA 2321218	AA	19990819	CA 1999-2321218	19990211
AU 9924287	A1	19990830	AU 1999-24287	19990211
EP 1054882	A1	20001129	EP 1999-903732	19990211
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2002503659	T2	20020205	JP 2000-531443	19990211

PRIORITY APPLN. INFO.: FR 1998-1762 A 19980213
US 1998-81577P P 19980414
WO 1999-FR298 W 19990211

OTHER SOURCE(S): MARPAT 131:170268
GI



I



II

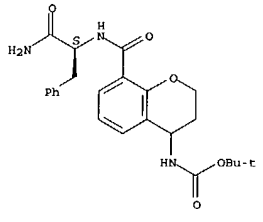
AB The invention concerns novel title compds. I, their preparation, pharmaceutical compns., and use for preparing medicines [wherein R1 = COCH(NH2)CH2SH, CH2CH(NH2)CH2SH, or CHRi1Ri2; R2 = H, alkyl, aralkyl, aryl, alkylcarbonyl, aralkylcarbonyl, arylcarbonyl, or heteroaralkyl; R3 = H, halo, alkyl, aryl, aralkyl; R4 = CHRi3Ri4; R5 = H, CORi5; R6 = H, alkyl, aryl, aralkyl; R7, R8 = H, alkyl, aryl, or aralkyl; X = O, S, S(O), S(O)2; Ri1 = (un)substituted heterocyclyl; Ri2 = H, alkyl, aryl, aralkyl; Ri3, Ri4 = H, (un)substituted aryl or heteroaryl (both ≠ H); Ri5 = OH, alkoxy, NH2, aralkylamino, alkylamino, NHCH(CO2Ri6)CH2CH2SMe; Ri6 = H, alkyl; including racemates stereoisomers, and salts]. The compds. are inhibitors of farnesyl transferase, and as such are potent antitumor and antileukemic agents. Examples include 86 syntheses, evaluation of the inhibition of farnesylation of K-ras in vitro, activity against human tumor cells (HCT116) in vitro [IC50 = 0.1 nM to 100 μM in both cases], and 3 pharmaceutical formulations. For instance, 4-chromanone underwent a sequence of reductive amination to the 4-amino compd. (50.4%), N-protection by BOC (95.3%), 8-lithiation and carboxylation (53.2%), peptide coupling with H-L-Phe-NH2 (93%), removal of BOC (28%), reductive amination with S-(triphenylmethyl)-N-BOC-L-cysteinal (87%), and final deprotection with Et3SiH and CF3CO2H, to give 2 diastereomers of title compd. II, isolated as the di(trifluoroacetate) salts.

L4 ANSWER 152 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

IT **238764-09-5P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(intermediate; preparation of aminochromancarboxamides and -thiochromancarboxamides as farnesyl transferase inhibitors)

RN 238764-09-5 CAPLUS
CN Carbamic acid, [8-[[[(1S)-2-amino-2-oxo-1-(phenylmethyl)ethyl]amino]carbonyl]-3,4-dihydro-2H-1-benzopyran-4-yl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 153 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:505653 CAPLUS
DOCUMENT NUMBER: 131:153742
TITLE: Bradykinin antagonists containing pentafluorophenylalanine, and therapeutic use
INVENTOR(S): Stewart, John M.; Gera, Lajos
PATENT ASSIGNEE(S): University Technology Corporation, USA
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5935932	A	19990810	US 1998-96716	19980612

PRIORITY APPLN. INFO.: US 1997-49571P P 19970613
OTHER SOURCE(S): MARPAT 131:153742

AB Bradykinin antagonists containing pentafluorophenylalanine which are therapeutically useful are provided. Also provided are methods to antagonize bradykinin receptors in a mammal in need of such antagonism, comprising administering a bradykinin antagonist containing pentafluorophenylalanine. Further provided are methods to treat inflammation in a mammal in need of such inhibition, comprising administering a bradykinin antagonist containing pentafluorophenylalanine. Lastly, a method to treat cancer in a mammal in need of such inhibition comprises administering a bradykinin antagonist containing pentafluorophenylalanine.

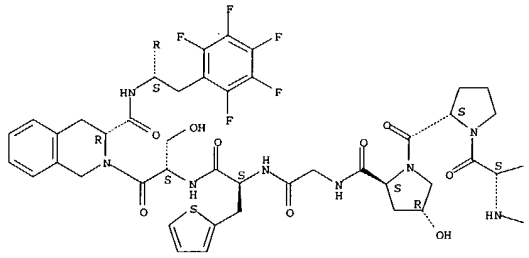
IT **236729-63-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(bradykinin antagonists containing pentafluorophenylalanine, and therapeutic use)

RN 236729-63-8 CAPLUS
CN L-Arginine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-3-(2-thienyl)-L-alanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-2,3,4,5,6-pentafluoro-L-phenylalanyl- (9CI) (CA INDEX NAME)

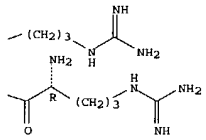
Absolute stereochemistry.

L4 ANSWER 153 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A

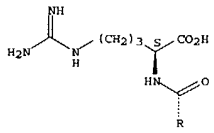


PAGE 1-B



L4 ANSWER 153 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 154 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:487274 CAPLUS
DOCUMENT NUMBER: 131:116520
TITLE: Preparation of phenylalanine derivatives as pharmaceutical agents
INVENTOR(S): Head, John Clifford; Archibald, Sarah Catherine; Warrellow, Graham John; Porter, John Robert
PATENT ASSIGNEE(S): Celltech Therapeutics Limited, UK
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9937618	A1	19990729	WO 1999-GB279	19990127
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6329372	B1	20011211	US 1999-237060	19990126
AU 9924320	A1	19990809	AU 1999-24320	19990127
EP 1051399	A1	20001115	EP 1999-903798	19990127
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2002501051	T2	20020115	JP 2000-528542	19990127
US 2002035127	A1	20020321	US 2001-964161	20010926

PRIORITY APPLN. INFO.: GB 1998-1674 A 19980127
GB 1998-26669 A 19981203
US 1999-237060 A1 19990126
WO 1999-GB279 W 19990127

OTHER SOURCE(S): MARPAT 131:116520

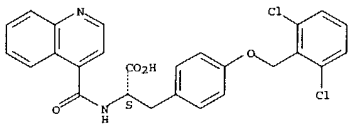
AB Phenylalanine derivs. 4-[R1(Alk1)rL1s]C6H2RaRb(Alk2)mCHRR2NR3COHet [R is a carboxylic acid or derivative; R1 = H, OH, alkoxy or optionally substituted cycloaliph., polycycloaliph., heterocycloaliph., polyheterocycloaliph., arom, or heteroarom. group; Alk1 = optionally substituted aliphatic or heteroaliph. chain; L1 is a linker atom or group; r, s = 0, 1; Ra, Rb = -L2(CH2)pL3Rcq, where L2, L3 = a covalent bond or linker atom or group; p = 0, 1; q = 1-3; Rc = H, halo, alkyl, OH, alkoxy, etc.; Alk2 = alkylene; m = 0, 1; R2 = H, Me; R3 = H, alkyl; Het is an optionally substituted heteroarom. group] and their salts, solvates, hydrates and N-oxides were prepared as pharmaceutical agents. Thus, N-(2-chloronicotinoyl)-N'-(3,5-dichloro-4-picolyl)-L-4-aminophenylalanine was prepared by coupling reaction of N-(3,5-dichloro-4-picolyl)-L-4-aminophenylalanine Me ester with 2-chloronicotinoyl chloride followed by ester hydrolysis. Title compds. were tested for inhibition of integrin-dependent cell adhesion and generally have IC50 values in the α4β1 and α4β7 assays of 1μM and below.

IT **232617-85-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of phenylalanine derivs. as pharmaceutical agents)

RN 232617-85-5 CAPLUS

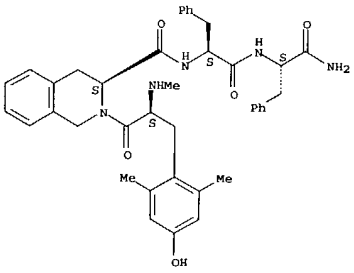
L4 ANSWER 154 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CN L-Tyrosine, O-[(2,6-dichlorophenyl)methyl]-N-(4-quinolinylcarbonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 155 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

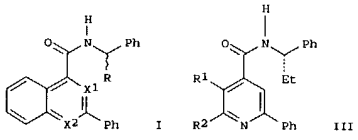


REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 155 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:484863 CAPLUS
DOCUMENT NUMBER: 131:266894
TITLE: The Opioid μ Agonist/δ Antagonist DIPP-NH2[Ψ] Produces a Potent Analgesic Effect, No Physical Dependence, and Less Tolerance than Morphine in Rats
AUTHOR(S): Schiller, Peter W.; Fundytus, Marian E.; Merovitz, Lisa; Weltrowska, Grazyna; Nguyen, Thi M.-D.; Lemieux, Carole; Chung, Nga N.; Coderre, Terence J.
CORPORATE SOURCE: Laboratory of Chemical Biology and Peptide Research and Pain Mechanisms Laboratory, Clinical Research Institute of Montreal, Montreal, QC, H2W 1R7, Can.
SOURCE: Journal of Medicinal Chemistry (1999), 42(18), 3520-3526
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Opioid compds. with mixed μ agonist/δ antagonist properties are expected to be analgesics with low propensity to produce tolerance and dependence. In an effort to strengthen the μ agonist component of the mixed μ agonist/δ antagonist H-Tyr-Tic-Phe-Phe-NH2 (TIPP-NH2), analogs containing structurally modified tyrosine residues in place of Tyr1 were synthesized. Among the prepared compds., H-Dmt-Tic-Phe-Phe-NH2 (DIPP-NH2; Dmt = 2',6'-dimethyltyrosine) and H-Dmt-TicΨ[CH2NH]Phe-Phe-NH2 (DIPP-NH2[Ψ]) retained a mixed μ agonist/δ antagonist profile, as determined in the guinea pig ileum and mouse vas deferens assays, whereas H-Tmt-Tic-Phe-Phe-NH2 (Tmt = N,2',6'-trimethyltyrosine) was a partial μ agonist/δ antagonist and H-Tmt-TicΨ[CH2NH]Phe-Phe-NH2 was a μ antagonist/δ antagonist. DIPP-NH2[Ψ] showed binding affinities in the subnanomolar range for both μ and δ receptors in the rat brain membrane binding assays, thus representing the first example of a balanced μ agonist/δ antagonist with high potency. In the rat tail flick test, DIPP-NH2[Ψ] given icv produced a potent analgesic effect (ED50 = 0.04 μg), being about 3 times more potent than morphine (ED50 = 0.11 μg). It produced less acute tolerance than morphine but still a certain level of chronic tolerance. Unlike morphine, DIPP-NH2[Ψ] produced no phys. dependence whatsoever upon chronic administration at high doses (≤4.5 μg/h) over a 7-day period. In conclusion, DIPP-NH2[Ψ] fulfills to a large extent the expectations based on the mixed μ agonist/δ antagonist concept with regard to analgesic activity and the development of tolerance and dependence.
IT **245538-28-7P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(opioid μ agonist/δ antagonist DIPP-NH2[Ψ] produces a potent analgesic effect and No phys. dependence and less tolerance than morphine in Rats in relation to structure)
RN 245538-28-7 CAPLUS
CN L-Phenylalaninamide, N,2,6-trimethyl-L-tyrosyl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

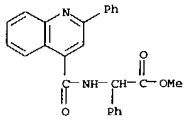
Absolute stereochemistry.

L4 ANSWER 156 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:470677 CAPLUS
DOCUMENT NUMBER: 131:228622
TITLE: Replacement of the quinoline system in 2-phenyl-4-quinolinecarboxamide NK-3 receptor antagonists
AUTHOR(S): Giardina, G. A. M.; Artico, M.; Cavagnera, S.; Cerri, A.; Consolandi, E.; Gagliardi, S.; Graziani, D.; Grugni, M.; Hay, D. W. P.; Luttmann, M. A.; Mena, R.; Raveglia, L. F.; Rigolio, R.; Sarau, H. M.; Schmidt, D. B.; Zanoni, G.; Farina, C.
CORPORATE SOURCE: Department of Medicinal Chemistry, SmithKline Beecham S.p.A., Milan, 20021, Italy
SOURCE: Farmaco (1999), 54(6), 364-374
CODEN: FRMCE8; ISSN: 0014-827X
PUBLISHER: Elsevier Science S.A.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:228622
GI



AB Results from a medicinal chemical approach aimed at replacing the quinoline ring system in the potent and selective human neurokinin-3 (hNK-3) receptor antagonists (RS)-I (R = MeOCO, Et; X1 = C; X2 = N), (R)-I (R = MeOCO; X1 = C; X2 = N) and (S)-I (R = Et; X1 = C; X2 = N) are discussed. The data give further insight upon the potential NK-3 pharmacophore. In particular, it is highlighted that both the benzene-condensed ring and the quinoline nitrogen are crucial determinants for optimal binding affinity to the hNK-3 receptor. Some novel compds. I (R = MeOCO; X1 = X2 = C (II); R = MeOCO; X1 = X2 = N) and III (R1R2 = N:CHCH:N, CH2CH2CH2CH2) maintained part of the binding affinity to the receptor and compound II, featuring the naphthalene ring system, appears to be suitable for further modifications; it offers the option to introduce electron-withdrawing groups at position 2 and 4, conferring on the ring an overall electron-deficiency similar to that of the quinoline.
IT **174635-51-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(preparation, binding affinity and structure-activity relationship of NK-3 receptor antagonists)
RN 174635-51-9 CAPLUS
CN Benzeneacetic acid, α-[[(2-phenyl-4-quinolinyl)carbonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 156 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 157 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:454977 CAPLUS
DOCUMENT NUMBER: 131:194017
TITLE: Cyclic AMP phosphodiesterase inhibition by coumarins and furanocoumarins
AUTHOR(S): Sardari, Soroush; Nishibe, S.; Horita, K.; Nikaido, T.; Daneshtalab, M.
CORPORATE SOURCE: School Pharmaceutical Sciences, Health Sciences Univ. Hokkaido, Hokkaido, Japan
SOURCE: Pharmazie (1999), 54(7), 554-556
CODEN: PHARAT; ISSN: 0031-7144
PUBLISHER: Govi-Verlag Pharmazeutischer Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

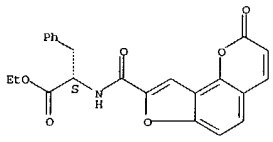
AB The phosphodiesterase inhibitory property of several synthetic as well as natural coumarins is reported. In comparison to caffeine, many of the coumarins tested showed strong inhibitory activity on phosphodiesterase. A comparison among the coumarins revealed that lipophilicity and the presence of a phenolic hydroxyl group at position 6 or 7 are 2 important factors in the phosphodiesterase inhibitory activity of coumarins.

IT **222640-31-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(cAMP phosphodiesterase inhibition by coumarins and furanocoumarins)

RN 222640-31-5 CAPLUS

CN L-Phenylalanine, N-[(2-oxo-2H-furo[2,3-h]-1-benzopyran-8-yl)carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



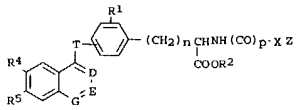
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 158 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

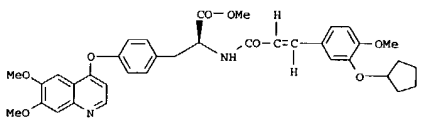
ACCESSION NUMBER: 1999:439520 CAPLUS
DOCUMENT NUMBER: 131:102538
TITLE: Preparation of quinoline, isoquinoline, cinnoline and tyrosine derivatives as antiinflammatory and anti-allergy agents
INVENTOR(S): Nakao, Toyoo; Takei, Masao; Fukamachi, Hiromi; Ohashi, Hiroshi
PATENT ASSIGNEE(S): Kirin Brewery Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 40 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 11189586	A2	19990713	JP 1997-358639	19971225
PRIORITY APPLN. INFO.:			JP 1997-358639	19971225

OTHER SOURCE(S): MARPAT 131:102538
GI



I



II

AB Title compds. [I; T = O at 4, 3 position; R1 = H, 3-I, 3-Cl, 3-F, 3-OMe; R4 = H, OMe; R5 = H, OMe; G = N, CH; E = CH, N; D = CH, N; R2 = Et, Me; n = 0, 1; p = 1, 0; X = bond, CH2CH2, CH:CH, O, CH2, (CH2)10, (CH2)3, (CH2)6; Z = H, Bu-t, (un)substituted benzene, 1-naphthyl, 2-naphthyl,3-quinolinyl] are prepared as antiinflammatory agents and anti-allergy agents. Thus, title compound II was prepared from reaction product of isovanillic acid, cyclopentyl bromide, acetic acid, (triphenylphosphoranylidene)-, Me ester, and L-Tyrosine, O-(1,1-dimethylethyl)-, Me ester with addition cyclization reaction product of 3,4-Dimethoxyaniline and propanedioic acid, (ethoxymethylene)-, di-Et ester (EtOCOC(:CHOEt)COOEt).

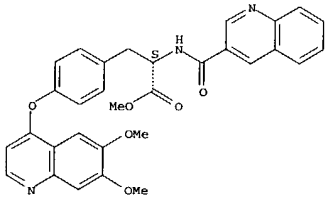
IT **231634-29-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

L4 ANSWER 158 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of quinoline, isoquinoline, cinnoline and amino acid derivs. as antiinflammatory and anti-allergy agents)

RN 231634-29-0 CAPLUS

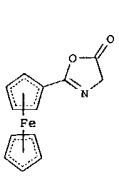
CN L-Tyrosine, O-(6,7-dimethoxy-4-quinolinyl)-N-(3-quinolinylcarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 159 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:405937 CAPLUS
DOCUMENT NUMBER: 131:199816
TITLE: Metal complexes of biologically important ligands. CXIV. Ferrocenyl-oxazolones as N and C donors in Pd(II), Pt(II) and Ir(III) complexes and ferrocenoyl-dipeptides
AUTHOR(S): Bauer, Werner; Polborn, Kurt; Beck, Wolfgang
CORPORATE SOURCE: Institut fur Anorganische Chemie, Ludwig-Maximilians-Universitat, Munchen, D-81377, Germany
SOURCE: Journal of Organometallic Chemistry (1999), 579(1-2), 269-279
CODEN: JORCAI; ISSN: 0022-328X
PUBLISHER: Elsevier Science S.A.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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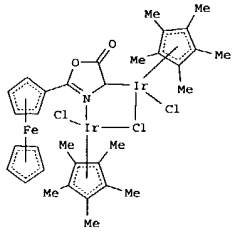


II

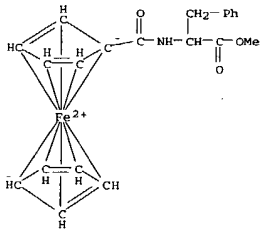
AB 2-Ferrocenyl-4R-5(4H)-oxazolones, e.g. I, were obtained from N-ferrocenoyl-α-amino acids and function as N donors in dichloro-phosphine-palladium(II) and platinum(II) complexes. The reaction of ferrocenyl-oxazolone and ferrocenyl-bis(oxazolone) with [Cp*IrCl2]2 afforded trimetallic and pentametallic complexes, e.g. II, with a C,N bridging oxazolone. Ring opening of the ferrocenyl-oxazolones with α-amino acid esters gave N-ferrocenoyl-dipeptide esters. In the ferrocene bis(dipeptides) the two peptide esters are aligned parallel by hydrogen bonding. The structures of platinum complex of ferrocenyl-oxazolone and II were determined by x-ray diffraction.

IT **181589-81-1P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and saponification of)

RN 181589-81-1 CAPLUS

CN Ferrocene, [[[(1S)-2-methoxy-2-oxo-1-(phenylmethyl)ethyl]amino]carbonyl]-

L4 ANSWER 159 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(9CI) (CA INDEX NAME)



REFERENCE COUNT: 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 160 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:404983 CAPLUS
DOCUMENT NUMBER: 131:45107
TITLE: Preparation of peptidyl antipicornaviral compounds
INVENTOR(S): Webber, Stephen E.; Dragovich, Peter S.; Prins, Thomas J.; Littlefield, Ethel S.; Marakovits, Joseph T.; Babine, Robert E.
PATENT ASSIGNEE(S): Agouron Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 187 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9931122	A1	19990624	WO 1998-US26583	19981215
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 5962487	A	19991005	US 1997-991739	19971216
CA 2312940	AA	19990624	CA 1998-2312940	19981215
AU 9918262	A1	19990705	AU 1999-18262	19981215
AU 762682	B2	20030703		
EP 1037905	A1	20000927	EP 1998-963184	19981215
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9813651	A	20001003	BR 1998-13651	19981215
JP 2002508389	T2	20020319	JP 2000-539045	19981215
NO 2000003067	A	20000815	NO 2000-3067	20000615

PRIORITY APPLN. INFO.: US 1997-991739 A 19971216
WO 1998-US26583 W 19981215

OTHER SOURCE(S): MARPAT 131:45107

AB Picornaviral 3C protease inhibitors R8R4NCR3R6C(:M)NR7CR2R5CR1:CZZ1 [M = O, S; R1 = H, F, alkyl, OH, SH, O-alkyl group; R2, R5 = H, alkyl, X-Y1-A1(B1)D1, X-Y2-A2(B2)D2 (X = :CH, :CF, CH2, CF2, CHF, S; Y1, Y2 = :CH, :CF; or X and Y1 or Y2 may form a ring; A1, A2 = C, CH, CF, S, P, Se, N, etc.; D1 and D2 are moieties with a lone pair of electrons capable of forming a hydrogen bond; B1, B2 = H, F, alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, etc.), R3, R6 = H, F, alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, CHO, OH, SH, etc.; R4 is any suitable organic moiety or R4 and R3 or R6 may form a ring; R7, R8 = H, alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, etc. or R4 and R8 may form a ring; Z, Z1 are H, F, alkyl, cycloalkyl, heterocycloalkyl, aryl, heteroaryl, etc.] were prepared Thus, Et 3-(Cbz-L-N-Me-Phe-L-Gln)-E-propenoate (Cbz = benzyloxycarbonyl) was prepared and showed Ki >100 μM for inhibition of Rhinovirus protease.

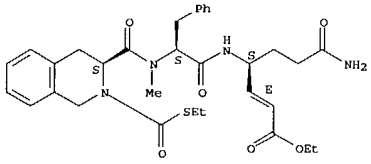
IT **227613-70-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptidyl antipicornaviral compds.)

RN 227613-70-9 CAPLUS

CN 2-Heptenoic acid, 7-amino-4-[[(2S)-2-[[[(3S)-2-[(ethylthio)carbonyl]-1,2,3,4-tetrahydro-3-isoquinolinyl]carbonyl]methylamino]-1-oxo-3-

L4 ANSWER 160 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
phenylpropyl]amino]-7-oxo-, ethyl ester, (2E,4S)- (9CI) (CA INDEX NAME)

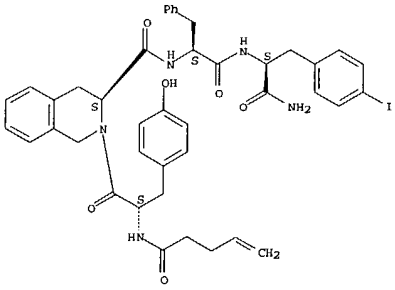
Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 161 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:396525 CAPLUS
DOCUMENT NUMBER: 131:200018
TITLE: Synthesis of conformationally constrained peptides using the Heck reaction
AUTHOR(S): Wright, David E.
CORPORATE SOURCE: R.W. Johnson Pharmaceutical Research Institute, San Diego, CA, 92121, USA
SOURCE: Peptides: Frontiers of Peptide Science, Proceedings of the American Peptide Symposium, 15th, Nashville, June 14-19, 1997 (1999), Meeting Date 1997, 279-280. Editor(s): Tam, James P.; Kaumaya, Pravin T. P. Kluwer: Dordrecht, Neth. CODEN: 67UCAR
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A symposium report. Heck reaction was used to develop cyclic opiate peptides. Cyclization was carried out using a p-iodophenylalanine residue and an alkene group.
IT **241814-55-1**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of conformationally constrained cyclopeptides via Heck cyclization)
RN 241814-55-1 CAPLUS
CN L-Phenylalaninamide, N-(1-oxo-4-pentenyl)-L-tyrosyl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-phenylalanyl-4-iodo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

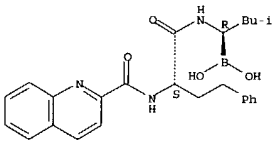


REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 162 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:368538 CAPLUS
DOCUMENT NUMBER: 131:153427
TITLE: Proteasome inhibitors: a novel class of potent and effective antitumor agents
AUTHOR(S): Adams, Julian; Palombella, Vito J.; Sausville, Edward A.; Johnson, Jill; Destree, Antonia; Lazarus, Douglas D.; Maas, Jochen; Pien, Christine S.; Prakash, Samuel; Elliott, Peter J.
CORPORATE SOURCE: ProScript, Inc., Cambridge, MA, 02139, USA
SOURCE: Cancer Research (1999), 59(11), 2615-2622 CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: AACR Subscription Office
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ubiquitin-proteasome pathway plays a critical role in the regulated degradation of proteins involved in cell cycle control and tumor growth. Dysregulating the degradation of such proteins should have profound effects on tumor growth and cause cells to undergo apoptosis. To test this hypothesis, we developed a novel series of proteasome inhibitors, exemplified by PS-341, which we describe here. As determined by the National Cancer Institute in vitro screen, PS-341 has substantial cytotoxicity against a broad range of human tumor cells, including prostate cancer cell lines. The PC-3 prostate cell line was, therefore, chosen to further examine the antitumor activity of PS-341. In vitro, PS-341 elicits proteasome inhibition, leading to an increase in the intracellular levels of specific proteins, including the cyclin-dependent kinase inhibitor, p21. Moreover, exposure of such cells to PS-341 caused them to accumulate in the G2-M phase of the cell cycle and subsequently undergo apoptosis, as indicated by nuclear condensation and poly(ADP-ribose) polymerase cleavage. Following weekly i.v. treatment of PS-341 to mice bearing the PC-3 tumor, a significant decrease (60%) in tumor burden was observed in vivo. Direct injection of PS-341 into the tumor also caused a substantial (70%) decrease in tumor volume with 40% of the drug-treated mice having no detectable tumors at the end of the study. Studies also revealed that i.v. administration of PS-341 resulted in a rapid and widespread distribution of PS-341, with highest levels identified in the liver and gastrointestinal tract and lowest levels in the skin and muscle. Modest levels were found in the prostate, whereas there was no apparent penetration of the central nervous system. An assay to follow the biol. activity of the PS-341 was established and used to determine temporal drug activity as well as its ability to penetrate tissues. As such, PS-341 was shown to penetrate PC-3 tumors and inhibit intracellular proteasome activity 1.0 h after i.v. dosing. These data illustrate that PS-341 not only reaches its biol. target but has a direct effect on its biochem. target, the proteasome. Importantly, the data show that inhibition of this target site by PS-341 results in reduced tumor growth in murine tumor models. Together, the results highlight that the proteasome is a novel biochem. target and that inhibitors such as PS-341 represent a unique class of antitumor agents. PS-341 is currently under clin. evaluation for advanced cancers.
IT **179324-59-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(development of potent, selective and reversible dipeptide boronic acid proteasome inhibitors as antitumor agents)

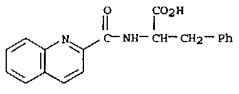
L4 ANSWER 162 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 179324-59-5 CAPLUS
CN Boronic acid, [(1R)-3-methyl-1-[[(2S)-1-oxo-4-phenyl-2-[(2-quinolinylcarbonyl)amino]butyl]amino]butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 163 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:332252 CAPLUS
DOCUMENT NUMBER: 131:88160
TITLE: Enantioselective solid-phase synthesis of α-amino acid derivatives
AUTHOR(S): O'Donnell, Martin J.; Delgado, Francisca; Pottorf, Richard S.
CORPORATE SOURCE: Department of Chemistry, Indiana University-Purdue University at Indianapolis, Indianapolis, IN, 46202, USA
SOURCE: Tetrahedron (1999), 55(20), 6347-6362 CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Wang-resin bound derivs. of glycine Schiff base esters are alkylated in the presence of quaternary ammonium salts derived from cinchonidine or cinchonine using phosphazene bases to give either enantiomer of the product α-amino acid derivs. in 51-89% ee.
IT **197392-59-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of in enantioselective solid-phase synthesis of α-amino acid derivs.)
RN 197392-59-9 CAPLUS
CN Phenylalanine, N-(2-quinolinylcarbonyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

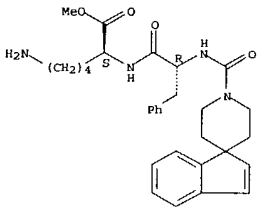
L4 ANSWER 164 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:317178 CAPLUS
DOCUMENT NUMBER: 130:325390
TITLE: Preparation of amino acid spiropiperidine derivatives as somatostatin agonists
INVENTOR(S): Guo, Liangquin; Mosley, Ralph T.; Pasternak, Alexander; Patchett, Arthur A.; Yang, Lihu
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9922735	A1	19990514	WO 1998-US22917	19981028
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9912854	A1	19990524	AU 1999-12854	19981028
US 6117880	A	20000912	US 1998-181590	19981028
PRIORITY APPLN. INFO.:			US 1997-64422P P	19971030
			GB 1998-6697 A	19980327
			WO 1998-US22917 W	19981028

OTHER SOURCE(S): MARPAT 130:325390
AB Title compds. R3R4NCOCR1R1aZ1ENR2 [NR2 represents spiro(indene-1,4'-piperidine) or spiro(indole-1,4'-piperidine) or related 2,3-dihydro derivs. in which the residue at the 3-position is CH2, CHCO2R2, CO, CHCH2CO2R2, CHCONR22, NSO2R2, or CR5 (R2 and R5 = H, alkyl, arylalkyl, cycloalkyl, etc.); R1 = alkyl, aryl, arylalkyl, heteroaryl, CO2R2, etc.; R1a = H, alkyl; R3 = H, alkyl, arylalkyl, heteroarylalkyl; R4 = CHCO2R2, CHCONR2, etc.; E = SO2, CO(CR22)n (n = 0-5), C(:NCN), C(:NNO2), C(:NSO2NR22); Z1 = NH, alkylimino, hydroxyalkylimino] were prepared as somatostatin agonists. Thus, R2NCO-D-Trp-NH(CH2)5NH2 [R2N = spiro(indene-1,4'-piperidine)] was prepared from reactions of D-tryptophan Me ester, spiro(indene-1,4'-piperidine), and 1,5-pentanediamine. The compds. of the invention inhibit the binding of somatostatin to its receptor at at IC50 of about 30 pM to about 3 μM.
IT **223770-91-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acid spiropiperidine derivs. as somatostatin agonists)
RN 223770-91-0 CAPLUS
CN L-Lysine, N-(spiro[1H-indene-1,4'-piperidin]-1'-ylcarbonyl)-D-phenylalanyl-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

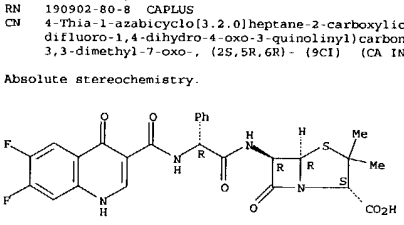
L4 ANSWER 164 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 165 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:314009 CAPLUS
DOCUMENT NUMBER: 131:129781
TITLE: Synthesis and antipseudomonal activity of fluoroquinolonyl-penicillin derivatives
AUTHOR(S): Tsou, Tai-Li; Tang, Shang-Tao; Wu, Jing-Ran; Hung, Yao-Wen; Liu, Yu-Tien
CORPORATE SOURCE: Institute of Preventive Medicine, National Defense Medical Center, Taipei, Taiwan
SOURCE: European Journal of Medicinal Chemistry (1999), 34(3), 255-259
CODEN: EJMCA5; ISSN: 0223-5234
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of ampicillin and amoxicillin derivs. containing an N1-substituted-(6-fluoro-1,4-dihydro-4-oxoquinolin-3-yl) carbonyl moiety at the α-amino group were prepared and their antibacterial activities were evaluated. These derivs. displayed a broad spectrum of antibacterial activity against Gram-(+) and Gram-(-) bacteria. In comparison with the original antibiotics, some of the derivs. were more active against Pseudomonas aeruginosa strains. However, their antibacterial activities decrease when N-1 substitution was replaced with alkyl substituents. Interestingly, several products induced filamentation in three strains of P. aeruginosa.
IT **190902-80-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and antipseudomonal activity of fluoroquinolonyl-penicillin derivs.)
RN 190902-80-8 CAPLUS
CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[(2R)-[[(6,7-difluoro-1,4-dihydro-4-oxo-3-quinolinyl)carbonyl]amino]phenylacetyl]amino]-3,3-dimethyl-7-oxo-, (2S,5R,6R)- (9CI) (CA INDEX NAME)

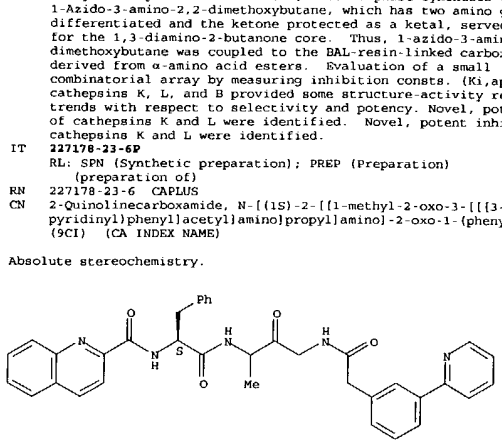
Absolute stereochemistry.



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 166 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:250927 CAPLUS
DOCUMENT NUMBER: 131:44415
TITLE: Solid-Phase Synthesis of a Combinatorial Array of 1,3-Bis(acylamino)-2-butanones, Inhibitors of the Cysteine Proteases Cathepsins K and L
AUTHOR(S): Yamashita, Dennis S.; Dong, Xiaoyang; Oh, Hye-Ja; Brook, Christopher S.; Tomaszek, Thaddeus A.; Szewczuk, Lawrence; Tew, David G.; Veber, Daniel F.
CORPORATE SOURCE: Departments of Medicinal Chemistry Molecular Recognition and Synthetic Chemistry, SmithKline Beecham Pharmaceuticals, King of Prussia, PA, 19406, USA
SOURCE: Journal of Combinatorial Chemistry (1999), 1(3), 207-215
CODEN: JCCHFF; ISSN: 1520-4766
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To more rapidly prepare members of the 1,3-bis(acylamino)-2-butanone class of cysteine protease inhibitors, a solid-phase synthesis was developed. 1-Azido-3-amino-2,2-dimethoxybutane, which has two amino groups differentiated and the ketone protected as a ketal, served as a surrogate for the 1,3-diamino-2-butanone core. Thus, 1-azido-3-amino-2,2-dimethoxybutane was coupled to the BAL-resin-linked carboxylic acids derived from α-amino acid esters. Evaluation of a small combinatorial array by measuring inhibition consts. (Ki,apps) against cathepsins K, L, and B provided some structure-activity relationship trends with respect to selectivity and potency. Novel, potent inhibitors of cathepsins K and L were identified. Novel, potent inhibitors of cathepsins K and L were identified.
IT **227178-23-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 227178-23-6 CAPLUS
CN 2-Quinolinecarboxamide, N-[(1S)-2-[[1-methyl-2-oxo-3-[[[3-(2-pyridinyl)phenyl]acetyl]amino]propyl]amino]-2-oxo-1-(phenylmethyl)ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

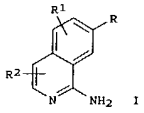
L4 ANSWER 167 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:184268 CAPLUS
DOCUMENT NUMBER: 130:223587
TITLE: 1-amino-7-isoquinoline derivatives as serine protease inhibitors
INVENTOR(S): Liebeschuetz, John Walter; Wylie, William Alexander; Waszkowycz, Bohdan; Murray, Christopher William; Rimmer, Andrew David; Welsh, Pauline Mary; Jones, Stuart Donald; Roscoe, Jonathan Michael Ernest; Young, Stephen Clinton; Morgan, Phillip John; Camp, Nicholas Paul; Crew, Andrew Philip Austin
PATENT ASSIGNEE(S): Proteus Molecular Design Ltd., UK
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 13
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9911657	A1	19990311	WO 1998-GB2600	19980828
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9888753	A1	19990322	AU 1998-88753	19980828
EP 1012166	A1	20000628	EP 1998-940425	19980828
EP 1012166	B1	20031029		
R: CH, DE, ES, FR, GB, IT, LI, NL				
US 6262069	B1	20010717	US 2000-485677	20000225
US 2002040144	A1	20020404	US 2001-865418	20010529
US 6420438	B1	20020716	US 2000-865418	20010529
US 2003216403	A1	20031120	US 2003-296245	20030514

PRIORITY APPLN. INFO.: GB 1997-18392 A 19970829
GB 1998-3173 A 19980213
WO 1998-GB2600 W 19980828
US 2000-485677 A1 20000225
WO 2001-GB2566 W 20010612

OTHER SOURCE(S): MARPAT 130:223587
GI



I

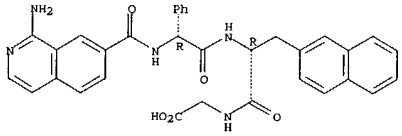
L4 ANSWER 167 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

AB Aminoisoquinoline amino acid derivs. I [R1 = H, halo, cyano, nitro, hydroxy, amino, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, thiol, alkylthio, aminosulfonyl, alkoxyalkyl, alkoxycarbonyl, acyloxymethoxycarbonyl or alkylamino (optionally substituted); R2 = H, halo, Me, amino, hydroxy, or oxo; and R is X-X-Y(R7)-L-Lp(D)n, where each X independently is a C, N, O or S atom or a CO, CR1, CR12 or NR1 group; Y is a nitrogen atom or a CR1 group or Y and L taken together form a cyclic group; R7 is a lipophilic group selected from alkyl, alkenyl, mono- or bi-cycloalkyl, aryl, heteroaryl, mono- or bicycloalkylalkyl, mono- or bicycloalkylalkenyl, aralkyl, heteroaryl-alkyl, arylalkenyl, heteroarylalkenyl, all optionally substituted by a group R1; L is an organic linker group containing 1 to 5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; Lp is a lipophilic organic group selected from alkyl, heterocyclic, alkenyl, alkaryl, cycloalkyl, polycycloalkyl, cycloalkenyl, aryl, aralkyl or haloalkyl group or a combination of two or more such groups optionally substituted by one or more of oxa, thia, aza or R1 groups; D is a hydrogen bond donor group; and n is 0, 1, or 2] or their 3,4-dihydro derivs. were prepared as serine protease inhibitors. Thus, 1-aminoisoquinolin-7-oyl-D-phenylglycine-4-methoxybenzylamide was prepared by amidation of Boc-D-phenylglycine with 4-methylbenzylamine, followed by deprotection and coupling with 1-aminoisoquinoline-7-carboxylic acid trifluoroacetate.

IT **221049-79-2P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of aminoisoquinoline peptidyl derivs. as serine protease inhibitors)

RN 221049-79-2 CAPLUS
CN Glycine, (2R)-N-[(1-amino-7-isoquinolinyl)carbonyl]-2-phenylglycyl-3-(2-naphthalenyl)-D-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 168 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

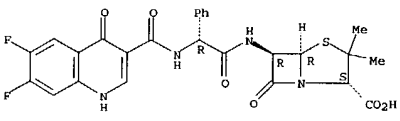
ACCESSION NUMBER: 1999:150027 CAPLUS
DOCUMENT NUMBER: 130:311633
TITLE: Synthesis and antibacterial activity of penicillin derivatives containing an (N1-substituted-6-fluoro-4-oxoquinolin-3-yl)carbonyl moiety
AUTHOR(S): Tsou, Tai-Li; Tang, Shang-Tao; Chang, Shu-Lin; Wu, Jing-Ran; Tarn, Lih-Jeng; Wu, Ching-Shei
CORPORATE SOURCE: Institute of Preventive Medicine, National Defense Medical Center, Taipei, Taiwan
SOURCE: Chinese Pharmaceutical Journal (Taipei) (1998), 50(6), 369-383
CODEN: CPHJEP; ISSN: 1016-1015
PUBLISHER: Pharmaceutical Society of Republic of China
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of ampicillin and amoxicillin derivs. containing an N1-substituted (6-fluoro-1,4-dihydro-4-oxoquinolin-3-yl)carbonyl moiety at the α-amino group were prepared and their antibacterial activities were evaluated. These derivs. displayed a broad spectrum of antibacterial activity against Gram (+) and Gram (-) bacteria. When comparison to the original antibiotics, some of the derivs. were more active against Pseudomonas aeruginosa, Streptococcus pyogenes, and β-lactamase producing Staphylococcus aureus strains. The MICs ranged from 3.2 to 13 μg/mL for P. aeruginosa and from 0.0062 to 0.05 μg/mL for St. pyogenes. Their antibacterial activities decreased when the N-1 position was replaced with alkyl substituents.

IT **190902-80-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and antibacterial activity of 6-fluoroquinolonyl penicillin deriva.)

RN 190902-80-8 CAPLUS
CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[(2R)-[[(6,7-difluoro-1,4-dihydro-4-oxo-3-quinolinyl)carbonyl]amino]phenylacetyl]amino]-3,3-dimethyl-7-oxo-, (2S,5R,6R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 169 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

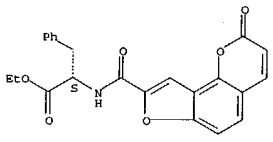
ACCESSION NUMBER: 1999:148078 CAPLUS
DOCUMENT NUMBER: 130:279176
TITLE: Antifungal activity of 2'-substituted furanocoumarins and related compounds
AUTHOR(S): Sardari, Soroush; Able, M.; Micetich, R. G.; Danesh-Talab, M.
CORPORATE SOURCE: Faculty Pharmacy Pharmaceutical Sciences, University Alberta, Edmonton, AB, Can.
SOURCE: Pharmazie (1999), 54(2), 156-158
CODEN: PHARAT; ISSN: 0031-7144
PUBLISHER: Govi-Verlag Pharmazeutischer Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The antifungal activity of several 2'-substituted furanocoumarins and 7-substituted coumarins against Candida albicans, Cryptococcus neoformans, Saccharomyces cerevisiae, and Aspergillus niger was tested. Strong antifungal activities were shown by angelicin, 2'-NO2-furanocoumarin as well as the coumarins containing propylamine, decylamine, hexadecylamine, and 11-amino-undecanoic acid Et ester. The 2'-carboxamido-furanocoumarins containing propylamine, decylamine, and hexadecylamine as amino component had also antifungal activity. The min. inhibitor concns. were listed.

IT **222640-31-5**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(antifungal activity of 2'-substituted furanocoumarins and related compds.)

RN 222640-31-5 CAPLUS
CN L-Phenylalanine, N-[(2-oxo-2H-furo[2,3-h]-1-benzopyran-8-yl)carbonyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 170 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

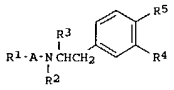
ACCESSION NUMBER: 1999:139868 CAPLUS
DOCUMENT NUMBER: 130:196958
TITLE: Preparation of 3-tert-butyl-L-tyrosinamide-containing peptides and related compounds exhibiting a motilin receptor antagonism
INVENTOR(S): Kotake, Ken-ichiro; Kozono, Toshiro; Sato, Tsutomu; Takanashi, Hisanori
PATENT ASSIGNEE(S): Chugai Seiyaku Kabushiki Kaisha, Japan
SOURCE: PCT Int. Appl., 144 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9909053	A1	19990225	WO 1998-JP3627	19980814
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
TW 460478	B	20011021	TW 1998-87113211	19980811
CA 2301687	AA	19990225	CA 1998-2301687	19980814
AU 9886490	A1	19990308	AU 1998-86490	19980814
AU 741216	B2	20011129		
JP 2000044595	A2	20000215	JP 1998-229586	19980814
EP 1006122	A1	20000607	EP 1998-937826	19980814
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6255285	B1	20010703	US 2000-485620	20000215

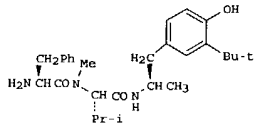
PRIORITY APPLN. INFO.: JP 1997-255879 A 19970815
JP 1998-186802 A 19980528
WO 1998-JP3627 W 19980814

OTHER SOURCE(S): MARPAT 130:196958
GI

L4 ANSWER 170 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



I



II

AB Phenethylamine derivs. represented by general formula [I; wherein A represents an amino acid or α-substituted amino acid residue; R1 represents R6CO, (un)substituted C2-7 linear or branched alkyl, C3-8 alkenyl, or C3-8 alkynyl; R2 represents hydrogen, C1-3 linear or branched alkyl; R3 represents COR7, (un)substituted C1-5 linear or branched alkyl, C2-5 alkenyl, or C2-5 alkynyl; R4 represents H, C1-6 linear or branched alkyl, C2-6 alkenyl, C2-6 alkynyl, etc.; R5 represents hydroxy or C1-4 n-alkoxy; R6 represents (un)substituted C1-6 linear or branched alkyl, C2-7 alkenyl, or C2-7 alkynyl, optionally benzene- or heterocyclic ring-condensed C3-7 cycloalkyl, (un)substituted C6-12 aromatic ring, (un)substituted C3-12 (un)saturated heterocyclic ring, (un)substituted NH2, (un)substituted linear or branched C1-5 alkoxy, C2-6 alkenyloxy, C2-6 alkynyloxy, etc.; and R7 represents H, (un)substituted C1-5 linear or branched alkyl, C3-7 cycloalkyl, (un)substituted NH2, OH, linear or branched alkyl C1-6 alkoxy, or C3-7 cycloalkyloxy] are prepared Also claimed are a motilin receptor antagonist, an inhibitor of digestive tract motility, and a remedy for high blood motilin. They are also useful for the treatment of irritable bowel syndrome. Thus, Nα-methyl-N-[2-(3-tert-butyl-4-hydroxyphenyl)-1-methylethyl]-L-valinamide was condensed with Boc-Phe-OH using HOBT and DIC in DMF at room temperature for 2.5 days followed by deprotection with CF3CO2H in CH2Cl2 to give the title compound (II). II in vitro showed IC50 of 1.9 nM for inhibiting the binding of [125I]motilin motilin receptor preparation from rabbit ileum mucus membrane.

IT **220806-26-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 3-tert-butyl-L-tyrosinamide-containing peptide compds. as motilin receptor antagonists, inhibitors of digestive tract motility,

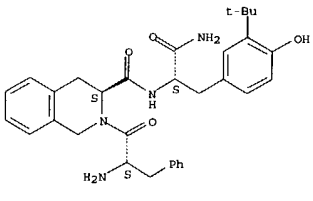
L4 ANSWER 170 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
and remedy for high blood motilin)

RN 220806-26-8 CAPLUS
CN L-Tyrosinamide, L-phenylalanyl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-3-(1,1-dimethylethyl)-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 220806-25-7
CMF C32 H38 N4 O4

Absolute stereochemistry.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 171 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

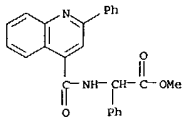
ACCESSION NUMBER: 1999:137688 CAPLUS
DOCUMENT NUMBER: 130:346848
TITLE: Discovery of a Novel Class of Selective Non-Peptide Antagonists for the Human Neurokinin-3 Receptor. 2. Identification of (S)-N-(1-Phenylpropyl)-3-hydroxy-2-phenylquinoline-4-carboxamide (SB 223412)
AUTHOR(S): Giardina, Giuseppe A. M.; Raveglia, Luca F.; Grugni, Mario; Sarau, Henry M.; Farina, Carlo; Medhurst, Andrew D.; Graziani, Davide; Schmidt, Dulcie B.; Rigolio, Roberto; Luttmann, Mark; Cavagnera, Stefano; Foley, James J.; Vecchietti, Vittorio; Hay, Douglas W. P.
CORPORATE SOURCE: Department of Medicinal Chemistry, SmithKline Beecham S.p.A., Baranzate, 20021, Italy
SOURCE: Journal of Medicinal Chemistry (1999), 42(6), 1053-1065
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Optimization of the previously reported 2-phenyl-4-quinolinecarboxamide NK-3 receptor antagonist with regard to potential metabolic instability of the ester moiety and affinity and selectivity for the human neurokinin-3 (hNK-3) receptor, is described. The ester functionality could be successfully replaced by the ketone or by lower alkyl groups (Et or n-Pr). Investigation of the substitution pattern of the quinoline ring resulted in the identification of position 3 as a key position to enhance hNK-3 binding affinity and selectivity for the hNK-3 vs. the hNK-2 receptor. All of the chemical groups introduced at this position, with the exception of halogens, increased the hNK-3 binding affinity, and SB 223412 (3-OH derivative, hNK-3-CHO binding Ki = 1.4 nM) and the 3-NH2 derivative (hNK-3-CHO binding Ki = 1.2 nM) were the most potent compds. of this series. Selectivity studies vs. the other neurokinin receptors (hNK-2-CHO and hNK-1-CHO) revealed that SB 223412 is about 100-fold selective for the hNK-3 vs. hNK-2 receptor, with no affinity for the hNK-1 at concns. ≤100 μM. In vitro studies demonstrated that SB 223412 is a potent functional antagonist of the hNK-3 receptor (reversal of senktide-induced contractions in rabbit isolated iris sphincter muscles and reversal of NKB-induced Ca2+ mobilization in CHO cells stably expressing the hNK-3 receptor), while in vivo this compound showed oral and i.v. activity in NK-3 receptor-driven models (senktide-induced behavioral responses in mice and senktide-induced miosis in rabbits). Overall, the biol. data indicate that SB 223412 [(S)-N-(1-phenylpropyl)-3-hydroxy-2-phenylquinoline-4-carboxamide] may serve as a pharmacol. tool in animal models of disease to assess the functional and pathophysiol. role of the NK-3 receptor and to establish therapeutic indications for non-peptide NK-3 receptor antagonists.

IT **174635-51-9P**
RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process); RACT (Reactant or reagent)
(discovery of a novel class of selective non-peptide antagonists for human neurokinin-3 receptor and identification of (S)(1-phenylpropyl)hydroxyphenylquinolinecarboxamide (SB 223412))

RN 174635-51-9 CAPLUS
CN Benzeneacetic acid, α-[[(2-phenyl-4-quinolinyl)carbonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 171 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

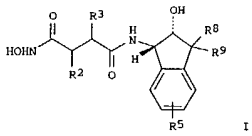


REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 172 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:136877 CAPLUS
DOCUMENT NUMBER: 130:209514
TITLE: Preparation of hydroxyindanylbutanediamides and related compounds as inhibitors of aggrecanase and matrix metalloproteinases for the treatment of arthritis.
INVENTOR(S): Yao, Wenqing; Decicco, Carl P.
PATENT ASSIGNEE(S): Du Pont Pharmaceuticals Company, USA
SOURCE: PCT Int. Appl., 251 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9909000	A2	19990225	WO 1998-US17048	19980818
WO 9909000	A3	19990910		
W: AU, BR, CA, CN, CZ, EE, HU, IL, JP, KR, LT, LV, MX, NO, NZ, PL, RO, SG, SI, SK, UA, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6576664	B1	20030610	US 1998-134484	19980814
ZA 9807376	A	20000217	ZA 1998-7376	19980817
CA 2301038	AA	19990225	CA 1998-2301038	19980818
AU 9890214	A1	19990308	AU 1998-90214	19980818
EP 1005448	A2	20000607	EP 1998-942083	19980818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EE 200000093	A	20001215	EE 2000-20000009	19980818
BR 9815596	A	20010102	BR 1998-15596	19980818
MX 200000956	A	20001020	MX 2000-956	20000127
NO 2000000784	A	20000407	NO 2000-784	20000217

PRIORITY APPLN. INFO.: US 1997-55944P P 19970818
US 1997-68335P P 19971219
WO 1998-US17048 W 19980818
OTHER SOURCE(S): MARPAT 130:209514
GI

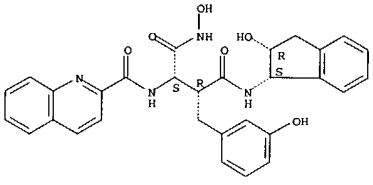


I

AB Title compds., e.g., [I; R2, R3, R5 = UXYZUaXaYaZa; U, Ua = null, O, CO,

L4 ANSWER 172 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
CO2, NRa, O2CNRa, OCO2, SOp, etc.; X, Xa = null, H, alkylene, alkenylene, alkynylene; Y, Ya = null, H, O, NRa, CO, SOp; Z, Za = null, H, (substituted) carbocyclyl, heterocyclyl; Ra = H, alkyl, Ph, PhCH2; R8, R9 = H, (substituted) alkyl, alkenyl, alkylaryl, carbocyclyl, heterocyclyl, etc.; R8R9C = atoms to form a heterocyclyl ring; p undefined], were prepd. as inhibitors of aggrecanase and matrix metalloproteinases (no data). Thus, (2R)-isobutyl-3-(tert-butoxycarbonyl)propanoic acid, (1S,2R)-cis-1-amino-2-indanol, TBTU, and (Me2CH)2NEt were stirred at 0° to room temp. to give 87% N1-(2R-hydroxy-1S-indanyl)-2R-isobutyl-3-(tert-butoxycarbonyl)propanamide. This in CH2Cl2/H2O was treated with CF3CO2H to give N-(2R-hydroxy-1S-indanyl)-2R-isobutyl-3-(hydroxycarbonyl)propanamide. The latter in DMF was treated with PhCH2ONH2.HCl, TBTU, and (Me2CH)2NEt at 0° to room temp. to give a product which was hydrogenolyzed in MeOH over Pd/BaSO4 to give N1-[2(R)-hydroxy-1(S)-indanyl]-N4-hydroxy-2(R)-isobutylbutanediamide.
IT **220682-81-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of hydroxyindanylbutanediamides and related compds. as inhibitors of aggrecanase and matrix metalloproteinases for the treatment of arthritis)
RN 220682-81-5 CAPLUS
CN Butanediamide, N1-[(1S,2R)-2,3-dihydro-2-hydroxy-1H-inden-1-yl]-N4-hydroxy-2-[(3-hydroxyphenyl)methyl]-3-[(2-quinolinylcarbonyl)amino]-, (2R,3S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 173 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:113708 CAPLUS
DOCUMENT NUMBER: 130:153982
TITLE: Preparation of N-sulfonyl phenylalanine dipeptide derivatives and analogs as inhibitors of leukocyte adhesion mediated by VLA-4
INVENTOR(S): Dappen, Michael S.; Dressen, Darren B.; Grant, Francine S.; Pleiss, Michael A.; Robinson, Cynthia Y.; Sarantakis, Dimitrios; Thorsett, Eugene D.
PATENT ASSIGNEE(S): Athena Neurosciences, Inc., USA; American Home Products Corporation
SOURCE: PCT Int. Appl., 190 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906433	A1	19990211	WO 1998-US15952	19980731
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9886786	A1	19990222	AU 1998-86786	19980731
EP 1001973	A1	20000524	EP 1998-938207	19980731
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9811569	A	20000919	BR 1998-11569	19980731
JP 2001512136	T2	20010821	JP 2000-505188	19980731
US 6559127	B1	20030506	US 1998-127533	19980731
NO 2000000451	A	20000323	NO 2000-451	20000128
US 2003166575	A1	20030904	US 2002-266889	20021007

PRIORITY APPLN. INFO.: US 1997-112010P P 19970731
US 1997-904416 A1 19970731
US 1998-127533 A3 19980731
WO 1998-US15952 W 19980731
OTHER SOURCE(S): MARPAT 130:153982
AB Disclosed are title compds. R1SO2NR2CHR3QCHR5COR6 [R1 = (un)substituted alkyl, (un)substituted aryl, (un)substituted cycloalkyl, (un)substituted heterocyclyl; R2 = H, any group R1; R1R2 may form (un)substituted heterocyclic ring; R3 = H, any group R1; R2R3 may form (un)substituted unsatd. heterocyclic ring; R5 = CH2X1; X1 = H, OH, optionally substituted acylamino, alkyl, aryloxy, aryl, aryloxyaryl, CO2H, carboxyalkyl, carboxyheteroaryl, etc.; Q = C(X)NR7; R7 = H, alkyl; X = O, S; R6 = NH2, (un)substituted alkoxy, (un)substituted cycloalkoxy, succinimidyloxy, adamantylamino, β-cholest-5-en-3-yloxy, NHOY, NH(CH2)pCO2Y, OCH2NR9R10; Y = H, (un)substituted alkyl, (un)substituted aryl; p = 1-8; R9 = (un)substituted CO-aryl; R10 = H, CH2CO2R11, NHSO2Z; R11 = alkyl; Z = (un)substituted alkyl, (un)substituted cycloalkyl, (un)substituted aryl, (un)substituted heteroaryl, (un)substituted heterocyclyl; and pharmaceutically acceptable salts thereof, with provisos] which bind VLA-4 (also referred to as integrin α4β1 and CD49d/CD29). Certain of these compds. also inhibit leukocyte adhesion and, in particular, leukocyte adhesion mediated by VLA-4. Such compds. are useful in the treatment of inflammatory diseases in a mammalian patient, e.g., human,

L4 ANSWER 173 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

wherein the disease may be, for example, asthma, Alzheimer's disease, atherosclerosis, AIDS dementia, diabetes, inflammatory bowel disease, rheumatoid arthritis, tissue transplantation, tumor metastasis and myocardial ischemia. The compds. can also be administered for the treatment of inflammatory brain diseases such as multiple sclerosis. Thus, reaction of Ts-Gly-OH (Ts = tosyl) with oxalyl chloride in CH2Cl2, followed by peptide coupling with L-phenylalanine benzyl ester tosylate and catalytic hydrogenolysis, gave desired title compd. Ts-Gly-Phe-OH. All prepd. compds. have IC50 ≤ 15 μM in a VLA-4 binding assay.

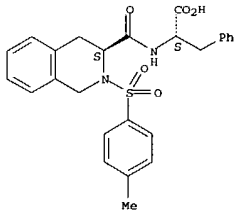
IT **220185-85-3P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of N-sulfonyl phenylalanine dipeptide derivs. and analogs as inhibitors of leukocyte adhesion mediated by VLA-4)

RN 220185-85-3 CAPLUS

CN L-Phenylalanine, N-[[(3S)-1,2,3,4-tetrahydro-2-[(4-methylphenyl)sulfonyl]-3-isoquinolinyl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 174 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:104519 CAPLUS
DOCUMENT NUMBER: 130:153971
TITLE: Preparation of tryptophan ureas as neurokinin antagonists
INVENTOR(S): Shah, Shrenik K.; Qi, Hongbo; Maccoss, Malcolm
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: U.S., 14 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5869489	A	19990209	US 1997-814387	19970311

PRIORITY APPLN. INFO.: US 1997-814387 19970311
OTHER SOURCE(S): MARPAT 130:153971
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Disclosed are substituted azacycles I [ring G = spirocycle Q1 or Q2, piperazine Q3, piperidine Q4; X = CH2, NSO2Me, NAc; R = Ph, 2-MeOC6H4, 2-MeC6H4, CH2Ph; R1 = Ph, R11 = NOMe [sic] (NHAc intended); R1 = H, R11 = CH2Ph, 1,2,3,4-tetrahydroquinazolin-2-on-1-yl; R2 = OCH2Ph wherein the Ph is optionally substituted with 1-3 substituents halo, Me, or CF3; N(R3)-C1-4 alkylphenyl, wherein the C1-4 alkyl may be linear or branched, the Ph is optionally substituted with 1-3 substituents halo, Me, MeO, or CF3; R3 = H, Me, Et] as tachykinin receptor antagonists useful in the treatment of inflammatory diseases, pain or migraine, and asthma. In particular compds. I are neurokinin antagonists. Thus, amidation of 1.967 g Boc-Trp-OH (Boc = Me3CO2C) with 0.87 mL MeNHCH2Ph gave 2.56 g of the corresponding amide, which underwent deprotection with CF3CO2H, condensation with carbonyldiimidazole, and urea formation with spiro[1H-indene-1,4'-piperidine] hydrochloride to give title compound II (L-743,516). II and related Trp derivs. showed IC50 values of >1000 to 1 nM for human neurokinin 1 (NK1) antagonist activity.

IT **199110-44-6P**

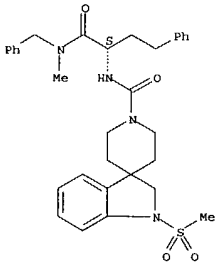
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of tryptophan ureas as neurokinin antagonists)

RN 199110-44-6 CAPLUS

CN Spiro[3H-indole-3,4'-piperidine]-1'-carboxamide, 1,2-dihydro-N-[(1S)-1-[[methyl(phenylmethyl)amino]carbonyl]-3-phenylpropyl]-1-(methylsulfonyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 174 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 175 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:96518 CAPLUS
DOCUMENT NUMBER: 130:153978
TITLE: Solid-phase synthesis of peptide CGRP-antagonists for use as medicaments
INVENTOR(S): Beck-Sickinger, Annette; Rist, Beate; Entzeroth, Michael
PATENT ASSIGNEE(S): Dr. Karl Thomae G.m.b.H., Germany
SOURCE: Ger. Offen., 20 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19732944	A1	19990204	DE 1997-19732944	19970731

PRIORITY APPLN. INFO.: DE 1997-19732944 19970731
OTHER SOURCE(S): MARPAT 130:153978
AB Variations on the r-CGRP-alpha-27-37 partial sequence H-F27-V28-P29-T30-N31-V32-G33-S34-E35-A36-F37-NH2 (see text for specifications) were prepared using solid-phase peptide synthesis techniques, for use in acute and prophylactic treatment of headache, non-insulin-dependent diabetes mellitus, cardiovascular disease, skin disease, inflammatory disease, allergic rhinitis, asthma, clotting disorders, and morphine tolerance (no data).

IT **220198-73-2P**

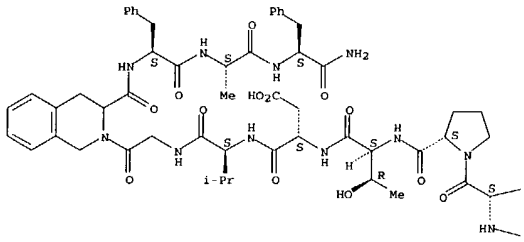
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of via solid-phase synthesis as CGRP-antagonists for use as medicaments)

RN 220198-73-2 CAPLUS

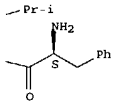
CN L-Phenylalaninamide, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-α-aspartyl-L-valylglycyl-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



L4 ANSWER 175 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 176 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

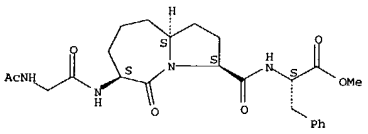
ACCESSION NUMBER: 1999:89647 CAPLUS
DOCUMENT NUMBER: 130:182766
TITLE: Conformational preferences of peptides containing reverse-turn mimetic bicyclic lactams. Inverse γ-turns versus type-II' β-turns. Insights into β-hairpin stability
AUTHOR(S): Belvisi, Laura; Gennari, Cesare; Mielgo, Antonia; Potenza, Donatella; Scolastico, Carlo
CORPORATE SOURCE: Dipartimento Chimica Organica Industriale, Univ. Studi Milano, Milan, Italy
SOURCE: European Journal of Organic Chemistry (1999), (2), 389-400
CODEN: EJOCFK; ISSN: 1434-193X
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The conformational preferences of constrained peptides containing reverse-turn mimetic bicyclic lactams were investigated by NMR and IR. The exptl. results were complemented by computer modeling studies and show that the constrained peptides form an inverse γ-turn or a type-II' β-turn through intramol. H-bonding, depending on the nature of the reverse-turn mimic. In N-acetylated tetrapeptide mimics incorporating the two different bicyclic lactams, H(5) is available for either a γ-turn (7-membered ring with the CO group of the bicyclic lactam) or a β-turn (10-membered ring with the CO group of residue 2). Peptides incorporating a (5,7)-bicyclic lactam predominantly induce the γ-turn conformation, while those incorporating a (5,6)-bicyclic lactam can promote either a γ-turn or a β-turn conformation, with the β-turn usually being preferred and with varying degrees of β-hairpin formation.

IT **220563-60-0**
RL: PRP (Properties)
(conformational anal.)

RN 220563-60-0 CAPLUS
CN L-Phenylalanine, N-acetylglycyl-(3S,6S,9aS)-6-aminooctahydro-5-oxo-1H-pyrrolo[1,2-a]azepine-3-carbonyl-, methyl ester (9CI) (CA INDEX NAME)

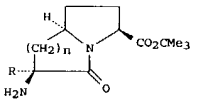
Absolute stereochemistry. Rotation (-).



REFERENCE COUNT: 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 177 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1999:89646 CAPLUS
DOCUMENT NUMBER: 130:196946
TITLE: Solid-phase synthesis of peptides containing reverse-turn mimetic bicyclic lactams
AUTHOR(S): Gennari, Cesare; Mielgo, Antonia; Potenza, Donatella; Scolastico, Carlo; Piarulli, Umberto; Manzoni, Leonardo
CORPORATE SOURCE: Dipartimento Chimica Organica Industriale, Univ. Studi Milano, Milan, Italy
SOURCE: European Journal of Organic Chemistry (1999), (2), 379-388
CODEN: EJOCFK; ISSN: 1434-193X
PUBLISHER: Wiley-VCH Verlag GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



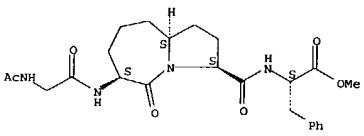
I

AB The solid-phase synthesis and characterization of a series of peptides containing reverse-turn mimetic bicyclic lactams I (n = 3, R = H; n = 2, R = PhCH2) is reported. The bicyclic lactams possess high structural similarity to the 2 central residues of a β-turn. Amino acid conjugates of these bicyclic lactams were synthesized on solid supports following a 9-fluorenylmethoxycarbonyl (FMOC) protection strategy on Wang-Merrifield resin. Coupling between amino acids was accomplished by diisopropylcarbodiimide (DIC)/hydroxyazabenzotriazole (HOAt). Coupling between amino acids and the mimics was performed with the potent Carpino's reagent, O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (HATU). The final compds. were cleaved from the resin and obtained as N-acetylated Me esters or benzyl amides.

IT **220563-60-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid-phase synthesis of peptides containing reverse-turn mimetic bicyclic lactams)

RN 220563-60-0 CAPLUS
CN L-Phenylalanine, N-acetylglycyl-(3S,6S,9aS)-6-aminooctahydro-5-oxo-1H-pyrrolo[1,2-a]azepine-3-carbonyl-, methyl ester (9CI) (CA INDEX NAME)

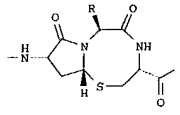
Absolute stereochemistry. Rotation (-).



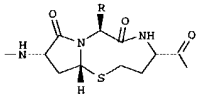
L4 ANSWER 177 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

REFERENCE COUNT: 90 THERE ARE 90 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 178 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:84975 CAPLUS
DOCUMENT NUMBER: 130:237857
TITLE: Bicyclic Tripeptide Mimetics with Reverse Turn Inducing Properties
AUTHOR(S): Johannesson, Petra; Lindeberg, Gunnar; Tong, Weimin; Gogoll, Adolf; Karlen, Anders; Hallberg, Anders
CORPORATE SOURCE: Department of Organic Pharmaceutical Chemistry, Uppsala University, Uppsala, SE-751 23, Swed.
SOURCE: Journal of Medicinal Chemistry (1999), 42(4), 601-608
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I



II

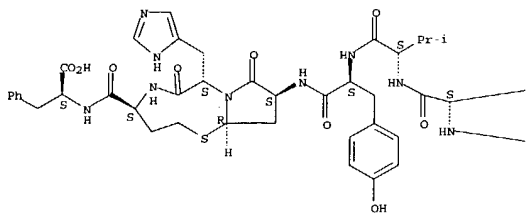
AB Analogs of the hypertensive octapeptide angiotensin II, comprising novel constrained 5,8-bicyclic and 5,9-bicyclic tripeptide units I and II (R = amino acid side chain) adopting nonclassical β-turn geometries, as deduced from theor. conformational anal., have been synthesized. Spontaneous bicyclization upon acid-catalyzed deprotection of a model peptide, encompassing a protected ω-formyl-α-amino acid in position 5 and Cys residues in positions 3 and 7, revealed a strong preference for bicyclization toward the C-terminus. The bicyclic thiazolidine related angiotensin II analogs synthesized exhibited no affinity for the angiotensin II AT1 receptor.

IT **221235-39-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of bicyclic tripeptide mimetics with reverse turn inducing properties)
RN 221235-39-8 CAPLUS
CN L-Phenylalanine, L-α-aspartyl-L-arginyl-L-valyl-L-tyrosyl-(αS)-α-[(3S,5R)-3-amino-5-mercapto-2-oxo-1-pyrrolidinyl]-1H-imidazole-4-propanoyl-L-homocysteinyl-, cyclic (5→6)-thioether (9CI) (CA INDEX NAME)

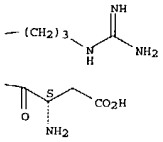
Absolute stereochemistry.

L4 ANSWER 178 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



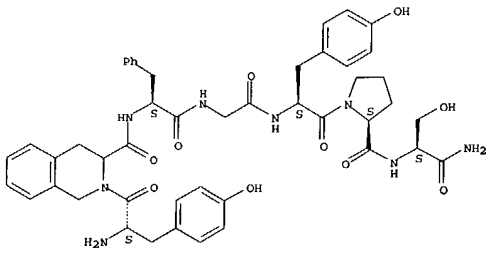
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 179 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:37202 CAPLUS
DOCUMENT NUMBER: 130:231893
TITLE: A uniform molecular model of δ opioid agonist and antagonist pharmacophore conformations
AUTHOR(S): Brandt, Wolfgang
CORPORATE SOURCE: Institute of Biochemistry, Martin-Luther-University Halle-Wittenberg, Halle, D-06099, Germany
SOURCE: Journal of Computer-Aided Molecular Design (1998), 12(6), 615-621
CODEN: JCADEQ; ISSN: 0920-654X
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB On the basis of a model of the pharmacophore conformations of agonist of the δ-opioid receptor the corresponding δ-antagonist conformations were determined by means of force field calcns. The results explain the unusual behavior of several cyclic β-casomorphin analogs on the mol. level. Thus, for instance, the model helps to understand why Tyr-c[D-Orn-2-Nal-D-Pro-Gly] is a mixed μ-agonist and δ-antagonist. Furthermore, the model is consistent with low energy conformations of other δ-antagonists such as Tyr-Tic-Phe, Tyr-Tic-Phe-Phe, naltrindole and BNTX. The occupation of a special spatial area by bulky groups close to the protonated N-terminus of opioid peptides is assumed to be highly critical for the switch from agonist to antagonist behavior.

IT **221333-35-3**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(uniform mol. model of δ-opioid agonist and antagonist pharmacophore conformations)
RN 221333-35-3 CAPLUS
CN Dermorphin, 2-(1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

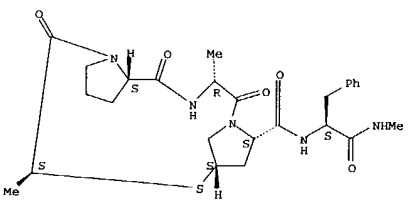
L4 ANSWER 180 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1999:4410 CAPLUS
DOCUMENT NUMBER: 130:139641
TITLE: Design, synthesis, structure and properties of an α-helix cap template derived from N-[(2S)-2-chloropropionyl]-(2S)-Pro-(2R)-Ala-(2S,4S)-4-thioPro-OMe which initiates α-helical structures
AUTHOR(S): Gani, David; Lewis, Arwel; Rutherford, Trevor; Wilkie, John; Stirling, Iain; Jenn, Thierry; Ryan, Martin D.
CORPORATE SOURCE: School of Chemistry and Centre for Biomolecular Science, The University, St. Andrews, Fife, KY16 9ST, UK
SOURCE: Tetrahedron (1998), 54(52), 15793-15819
CODEN: TETRAB; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A strategy based upon removing the requirement for all of the carbonyl dipoles to align at the same time in the transition state leading to the cyclization of N-[(2S)-2-chloropropionyl]-(2S)-Pro-(2R)-Ala-(2S,4S)-4-thioPro-OMe to a Zimm-Bragg type α-helix peptide initiator template was successful. Each amide bond of the 12-membered macrocyclic template existed in the trans-rotomeric form. Derivs. of the template were prepared by extending the C-terminus and these were characterized by NMR spectroscopy and restrained simulated annealing. In deuterochloroform solution at low temperature, sep. sets of NMR signals were observed for two rapidly interconverting helical conformational isomers of the thioether macrocycle which possessed an appended trialkylammonium ion. A similar time-averaged conformation was also observed in aqueous solution At -80° in d2-dichloromethane the rate of conformational exchange was slowed sufficiently to obtain resonance assignments and NOE data sep. for each isomer. In the minor isomer (40%), the four carbonyl oxygen hydrogen-bond acceptors of the template are aligned in an α-helical conformation and in the major conformer the Pro2 carbonyl dipole was anti-aligned with the other three dipoles. Thus, the conformers differ in the orientation of one carbonyl group. Mol. modeling calcns. showed that the minor isomer was stabilized by coulombic interactions between the trialkylammonium salt and the carbonyl group dipole moments.

IT **220061-81-4P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(design, synthesis, structure and properties of α-helix cap template)
RN 220061-81-4 CAPLUS
CN L-Phenylalaninamide, 1-[(2S)-2-mercapto-1-oxopropyl]-L-prolyl-D-alanyl-(4S)-4-mercapto-L-prolyl-N-methyl-, cyclic (1→3)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 180 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

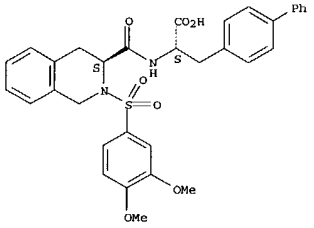


REFERENCE COUNT: 83 THERE ARE 83 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 181 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

CN [1,1'-Biphenyl]-4-propanoic acid, α-[[[(3S)-2-[(3,4-dimethoxyphenyl)sulfonyl]-1,2,3,4-tetrahydro-3-isoquinolinyl]carbonyl]amino]-, (αS)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 181 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:799995 CAPLUS
DOCUMENT NUMBER: 130:52736
TITLE: Preparation of biarylalkanoic acids as cell adhesion inhibitors
INVENTOR(S): Durette, Philippe L.; Hagmann, William K.; Maccoss, Malcolm; Mills, Sander G.; Mumford, Richard A.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9853817	A1	19981203	WO 1998-US10951	19980529
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9877031	A1	19981230	AU 1998-77031	19980529
AU 726585	B2	20001109		
EP 1017382	A1	20000712	EP 1998-924988	19980529
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2001517245	T2	20011002	JP 1999-500938	19980529
US 6291511	B1	20010918	US 1999-359015	19990722

PRIORITY APPLN. INFO.:
US 1997-47856P P 19970529
GB 1997-14316 A 19970707
US 1997-66831P P 19971125
GB 1998-680 A 19980114
US 1998-85793 B1 19980528
WO 1998-US10951 W 19980529

OTHER SOURCE(S): MARPAT 130:52736

AB Compds. R1YNR2CR3R4CONR5CR6R7X [R1 = (un)substituted alkyl, alkenyl, alkynyl, a cyclic group Cy, Cy-alkyl, Cy-alkenyl, Cy-alkynyl; R2, R3 independently are H or R1; or R2 and R3 together form a ring; R4, R7 independently are H, (un)substituted alkyl, alkenyl, alkynyl, aryl, arylalkyl, heteroaryl, or heteroarylalkyl; or R3 and R4 together form a ring; R5 = H or (un)substituted alkyl or Cy; R6 = diarylalkyl, -alkenyl, or -alkynyl; X = CO2H, PO3H2, PH(O)OH, SO2H, SO3H or ester derivs., carbamoyl group, or 5-tetrazolyl; Y = CO, OCO, NHCO or iminocarbonyl group, SO2, P(O)(ORi) (Ri =alkyl, alkenyl, alkynyl, aryl), COCO} were prepared as cell adhesion inhibitors. Pharmaceutical compns. are described. Thus, N-(3,5-dichlorobenzenesulfonyl)-L-prolyl-L-4-(4-fluorophenyl)phenylalanine was prepared by coupling of N-(3,5-dichlorobenzenesulfonyl)-L-proline with 4-iodo-L-phenylalanine and reaction with 4-fluorobenzeneboronic acid.

IT **217325-07-0P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptidyl biarylalkanoic acids as cell adhesion inhibitors)

RN 217325-07-0 CAPLUS

L4 ANSWER 182 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

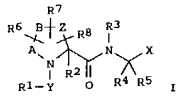
ACCESSION NUMBER: 1998:799992 CAPLUS
DOCUMENT NUMBER: 130:52724
TITLE: Preparation of heterocyclic dipeptide derivatives as cell adhesion inhibitors
INVENTOR(S): Durette, Philippe L.; Hagmann, William K.; Maccoss, Malcolm; Mills, Sander G.; Mumford, Richard A.; Van Riper, Gail M.; Schmidt, Jack A.; Kevin, Nancy J.
PATENT ASSIGNEE(S): Merck & Co., Inc., USA
SOURCE: PCT Int. Appl., 129 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9853814	A1	19981203	WO 1998-US10940	19980529
W: CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 1001764	A1	20000524	EP 1998-926122	19980529
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				
JP 2002512625	T2	20020423	JP 1999-500934	19980529
WO 9964395	A1	19991216	WO 1998-US11623	19980611
W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CN, CU, CZ, EE, GE, GW, HU, ID, IL, IS, KG, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9880595	A1	19991230	AU 1998-80595	19980611

PRIORITY APPLN. INFO.:
US 1997-48017P P 19970529
GB 1997-14314 A 19970707
US 1997-66525P P 19971125
GB 1998-686 A 19980114
WO 1998-US10940 W 19980529
WO 1998-US11623 A 19980611

OTHER SOURCE(S): MARPAT 130:52724

GI



I

AB Title compds. I [R1 = (un)substituted C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, Cy, Cy-C1-10 alkyl, Cy-C2-10 alkenyl, Cy-C2-10 alkynyl; R2, R5 = independently (un)substituted H, C1-10 alkyl, C2-10 alkenyl, C2-10 alkynyl, aryl, aryl-C1-10 alkyl, heteroaryl, heteroaryl-C1-10 alkyl; R3 = H, (un)substituted C1-10 alkyl, Cy, Cy-C1-10 alkyl; R4 = H, any group R1; R3R4 form mono- or bicyclic ring containing 0-2 heteroatoms N, O, S; R4R5 form 3-7 membered mono- or bicyclic ring containing 0-2 heteroatoms N, O, S; R10, R11 = independently = any group R3, (un)substituted C2-10 alkenyl, C2-10

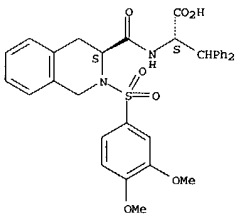
L4 ANSWER 182 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
alkynyl; R10R11 may form 5-7 membered heterocyclic ring contg. 0-2 addnl. heteroatoms N, O, S; R6-R8 = independently any group R10, OR10, NO2, halo, S(O)mR10, SR10, SO3R10, NR10R11, COR10, CO2R10, O2R10, CN, CONR10R11, CF3, oxo, NR10S(O)mR11, etc., two of R6-R8 may form 5-7 membered (un)satd. monocyclic ring contg. 0-3 heteroatoms N, O, S; Cy = cycloalkyl, heterocyclyl, aryl, heteroaryl; A, Z = independently C, C-C; B = bond, C, C-C, N, O, S, S(O)m; X = CO2R10, P(O)(OR10)(OR11), P(O)(R10)(OR11), S(O)mOR10, CONR10R11, 5-tetrazolyl; Y = CO, O2C, NR11CO, SO2, P(O)(OR4), COCO; m = 1-2] = are antagonists of VLA-4 and/or α4β7, and are useful for inhibition or prevention of cell adhesion and cell adhesion mediated pathologies. These compds. may be formulated into pharmaceutical compns. and are suitable for use in the treatment of asthma, allergies, inflammation, multiple sclerosis, and other inflammatory and autoimmune disorders. Thus, coupling of L-2-naphthylalanine tert-Bu ester (H-Nal-OtBu) (prepn. given) with Cbz-Pro-OH (Cbz = PhCH2O2C), followed by catalytic deprotection, sulfonylation with 3,5-Cl2C6H3SO2Cl, and acidic deesterification gave desired N-sulfonyldipeptide Cl2C6H3SO2-Nal-Pro-OH. Procedures for inhibition of VLA-4 dependent adhesion to a CS-1 conjugate and VCAM-IG fusion protein are given.

IT **217450-09-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of heterocyclic dipeptide derivs. as cell adhesion inhibitors)

RN 217450-09-4 CAPLUS

CN L-Phenylalanine, N-[[(3S)-2-[(3,4-dimethoxyphenyl)sulfonyl]-1,2,3,4-tetrahydro-3-isoquinolinyl]carbonyl]-β-phenyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 183 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:756613 CAPLUS
DOCUMENT NUMBER: 130:133637
TITLE: Side Chain Methyl Substitution in the δ-Opioid Receptor Antagonist TIPP Has an Important Effect on the Activity Profile
AUTHOR(S): Tourwe, Dirk; Mannekens, Els; Diem, Trang Nguyen Thi; Verheyden, Patricia; Jaspers, Hendrika; Toth, Geza; Peter, Antal; Kertesz, Istvan; Toeroek, Gabriella; Chung, Nga N.; Schiller, Peter W.
CORPORATE SOURCE: Eenheid Organische Chemie, Vrije Universiteit Brussel, Brussels, B-1050, Belg.
SOURCE: Journal of Medicinal Chemistry (1998), 41(26), 5167-5176
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The δ-opioid antagonist H-Tyr-Tic-Phe-Phe-OH (TIPP-OH) or its C-terminal amide analog was systematically modified topol. by substitution of each amino acid residue by all stereoisomers of the corresponding β-Me amino acid. The potency and selectivity (δ- vs μ- and κ-opioid receptor) were evaluated by radioreceptor binding assays. Agonist or antagonist potency were assayed in the mouse vas deferens and in the guinea pig ileum. In the TIPP analogs containing L-β-Me amino acids the influence on δ-receptor affinity and on δ-antagonist potency is limited, the [(2S,3R)-β-MePhe3]TIPP-OH analog being among the most potent δ-antagonists reported. In the D-β-Me amino acid series, the [D-β-MeTic2] analogs are δ-selective antagonists whereas [D-Tic2]TIPP-NH2 is a δ-agonist. NMR studies did not indicate any influence of the β-Me substituent on the conformation of the Tic residue. The [(2R,3S)-β-MePhe3]TIPP-NH2 is a potent δ-agonist, its C-terminal carboxylic acid analog being more δ-selective but displaying partial agonism in both the δ- and μ-bioassay. These results constitute further examples of a profound influence of β-Me substitution on the potency, selectivity, and signal transduction properties of a peptide.

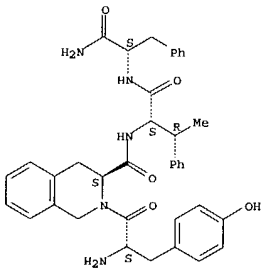
IT **174147-54-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(side chain Me substitution in the δ-opioid receptor antagonist TIPP has an important effect on the activity profile)

RN 174147-54-7 CAPLUS

CN L-Phenylalaninamide, L-tyrosyl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(βR)-β-methyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 183 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 184 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

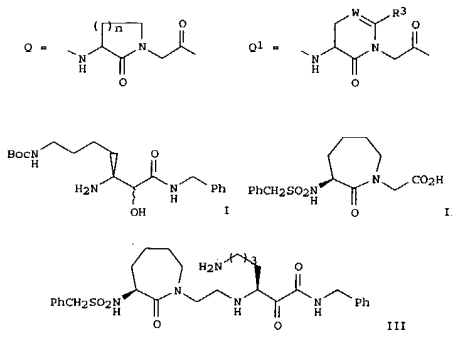
ACCESSION NUMBER: 1998:745086 CAPLUS
DOCUMENT NUMBER: 130:4091
TITLE: Preparation of backbone-cyclized peptide derivatives as serine protease and thrombin inhibitors
INVENTOR(S): Adang, Anton Egbert Peter
PATENT ASSIGNEE(S): Akzo Nobel N.V., Neth.
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9850420	A1	19981112	WO 1998-EP2587	19980428
W: AM, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, ID, IS, JP, KG, KP, KR, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9876520	A1	19981127	AU 1998-76520	19980428
AU 729910	B2	20010215		
EP 979240	A1	20000216	EP 1998-924265	19980428
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9809342	A	20000704	BR 1998-9342	19980428
NZ 500620	A	20001027	NZ 1998-500620	19980428
JP 2001524117	T2	20011127	JP 1998-547715	19980428
RU 2183642	C2	20020620	RU 1999-125967	19980428
ZA 9803629	A	19981104	ZA 1998-3629	19980429
US 6534495	B1	20030318	US 1999-403856	19991026
NO 9905316	A	19991101	NO 1999-5316	19991101
MX 9910057	A	20000731	MX 1999-10057	19991101

PRIORITY APPLN. INFO.: EP 1997-201286 A 19970502
WO 1998-EP2587 W 19980428

OTHER SOURCE(S): MARPAT 130:4091
GI

L4 ANSWER 184 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



AB The invention relates peptide derivs. R1SO2-B-X-Z-CO-Y [B = bond, amino acid NHCH[(CH2)pCO2H]CO or ester derivative thereof, Gly, D-1-perhydroisoquinolinecarboxylic acid (D-1-Piq), D-3-Piq, D-1,2,3,4-tetrahydroisoquinoline-1-carboxylic acid (D-1-Tiq), D-3-Tiq, D-aminotetralincarboxylic acid, aminoindanecarboxylic acid, L- or D-amino acid containing hydrophobic, basic, or neutral side chain; X = amino acid containing hydrophobic side chain, Gln, Ser, Thr, 2-aminoisobutyric acid, NR2CH2CO, Q, Q1, cyclic amino acid optionally containing addnl. heteroatom N, O or S, (un)substituted with C1-6 alkyl, C1-6 alkoxy, PhCH2O, oxo; Z = Lys, 4-aminocyclohexylglycine; Y = (un)substituted NHC1-6 alkylene-Ph, OR4, NR5R6; W = CH, N; R1 = R2O2C(CHR2)m, R2NH(CHR2)m, (un)substituted C1-12 alkyl, C2-12 alkenyl, C6-14 aryl, C7-15 aralkyl, C8-16 aralkenyl; each R2 = independently H, C1-12 alkyl, C3-8 cycloalkyl, (un)substituted C6-14 aryl or C7-15 aralkyl; R3 = H, C1-6alkyl, Ph optionally substituted with OH, C1-6 alkoxy, CO2H, CO2-C1-6 alkyl, CONH2, halo; R4 = H, C2-6 alkyl, CH2Ph; R5, R6 = independently H, C1-6 alkoxy, (un)substituted C1-6 alkyl; R5R6 = CH2CH2VCH2CH2; V = O, S, SO2; m = 1-3; n = 2-4; p = 1-3]. The compds. of the invention have anticoagulant activity and can be used in treating or preventing thrombin-related diseases. Thus, coupling of homologated Lys derivative I (prepared in 6 steps from Cbz-Lys(Boc)-OH, NaCN, and benzylamine) with backbone-cyclized dipeptide derivative II (prepared in 4 steps from L-α-amino-ε-caprolactam, Me bromoacetate, and benzylsulfonyl chloride), followed by oxidation and deprotection gave desired title compound III. III inhibited factor Xa with IC50 = 0.64 μM.

IT **215791-78-9P**

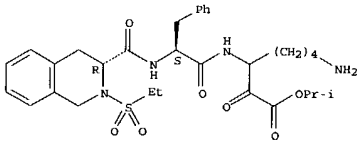
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

L4 ANSWER 184 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(prepn. of backbone-cyclized peptide derivs. as serine protease inhibitors)

RN 215791-78-9 CAPLUS

CN Heptanoic acid, 7-amino-3-[[(2S)-2-[[[(3R)-2-(ethylsulfonyl)-1,2,3,4-tetrahydro-3-isoquinolinyl]carbonyl]amino]-1-oxo-3-phenylpropyl]amino]-2-oxo-, 1-methylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 185 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:720328 CAPLUS

DOCUMENT NUMBER: 130:62593

TITLE: Equilibrium of the cis-trans isomerization of the peptide bond with N-alkyl amino acids measured by 2D NMR

AUTHOR(S): Misicka, Aleksandra; Verheyden, Patricia M. F.; Van Binst, Georges

CORPORATE SOURCE: Department of Chemistry, Warsaw University, Warsaw, PL-02-093, Pol.

SOURCE: Letters in Peptide Science (1998), 5(5-6), 375-377
CODEN: LPSCEM; ISSN: 0929-5666

PUBLISHER: Kluwer Academic Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The conformational cis-trans equilibrium around the peptide bond in model tripeptides has been determined by 2D NMR methods (HOHAHA, ROESY). The study was limited to three different NO-substituted amino acids in position 2, namely Pro (proline), Tic (1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid), and N-MePhe (N-methylphenyllalanine). In all cases the amino acid in position 1 was tyrosine and in position 3, phenylalanine. The results of our studies show that the cis-trans ratio depends mostly on the configuration of the amino acids forming the peptide bond undergoing the cis-trans isomerization. The amino acid following the sequence (in position 3) does not have much influence on the cis-trans isomerization, indicating that there is no interaction of the side chains between these amino acids. The model peptides with the L-Tyr_L-AA-(L- or D-)Phe (where AA is N-substituted amino acid) chiralities give 80-100% more of the cis form in comparison to the corresponding peptides with the D-Tyr-L-AA-(L- or D-)Phe chiralities. These results indicate that the incorporation of N-substituted amino acids in small peptides with the same chirality as the precedent amino acid involved in the peptide bond undergoing the cis/trans isomerization moves the equilibrium to a significant amount of the cis form.

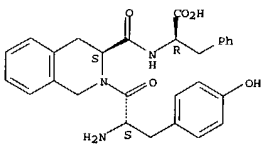
IT **217958-85-5**

RL: PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)
(equilibrium of cis-trans isomerization of peptide bond with N-alkyl amino acids measured by 2D NMR)

RN 217958-85-5 CAPLUS

CN D-Phenylalanine, L-tyrosyl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 186 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:720292 CAPLUS

DOCUMENT NUMBER: 130:61238

TITLE: The relationship between structure and activity among opioid peptides

AUTHOR(S): Deschamps, Jeffrey R.; George, Clifford; Flippen-Anderson, Judith L.

CORPORATE SOURCE: Laboratory for the Structure of Matter, Naval Research Laboratory, Washington, DC, 20375, USA

SOURCE: Letters in Peptide Science (1998), 5(5-6), 337-340
CODEN: LPSCEM; ISSN: 0929-5666

PUBLISHER: Kluwer Academic Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Since the discovery and isolation of the endogenous opioid peptides Leu- and Met-enkephalin, structural studies have been focused on deducing the bioactive conformation of the peptide ligands. Theor., linear peptides can have many different backbone conformations, yet early x-ray studies on enkephalin and its analogs showed only two different backbone conformations: extended and single β-bend. More recent reports include a third conformation for Leu-enkephalin and constrained opioid peptides from two "new" classes (i.e. cyclic and "all-aromatic" peptides). In this report the relationship between solid-state x-ray structure and opioid peptide activity is examined The N-terminal amine nitrogen and the two aromatic rings have previously been identified as structural features important to the biol. activity of opioid peptides. From x-ray studies we find that the distances between the centroids of the aromatic rings, and between the N-terminal amino nitrogen and the centroid of the phenylalanine ring, vary over a large range. There is a discernible relationship, however, between the separation of the two rings and their orientation that correlates with activity.

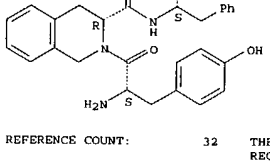
IT **217957-05-6**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(relationship between structure and activity among opioid peptides)

RN 217957-05-6 CAPLUS

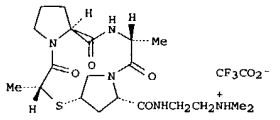
CN L-Phenylalanine, L-tyrosyl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 187 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:715819 CAPLUS
DOCUMENT NUMBER: 130:139618
TITLE: Design, construction and properties of peptide N-terminal cap templates devised to initiate α-helixes. Part 3. Caps derived from N-[(2S)-2-chloropropionyl]-(2S)-Pro-(2R)-Ala-(2S,4S)-4-thioPro-OMe
AUTHOR(S): Lewis, Arwel; Rutherford, Trevor J.; Wilkie, John; Jenn, Thierry; Gani, David
CORPORATE SOURCE: School of Chemistry and Centre for Biomolecular Sciences, The University St. Andrews, St. Andrews, Fife, KY16 9ST, UK
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1998), (22), 3795-3806
CODEN: JCPRB4; ISSN: 0300-922X
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

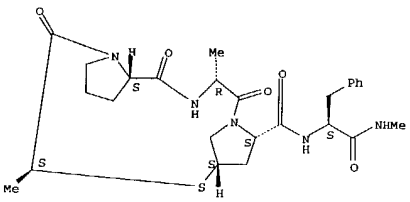


I

AB The construction of a 12-membered macrocyclic template capable of entraining attached peptides in helical conformations from acyclic tripeptide precursors derived from (S)-ClCHMeCO-Pro-Pro-(2S,4S)-4-thioPro-OMe has been severely hampered by the problem of simultaneously aligning carboxamide dipoles in the transition state for cyclization. Previously, the authors provided a detailed conformational anal. of the system and tested two methods for forcing the acyclic precursor into the macrocyclic conformation required for helix initiation. First, the destabilization of unwanted conformations in the transition state for cyclization, second, the stabilization of the favored transition state structure through the introduction of a hydrogen-bonding interaction. Both strategies were unsuccessful. A third strategy based upon removing the requirement for all of the carbonyl dipoles to align in the transition state at the same time was also tested and the results are presented here. The relaxation of the highly restrained Cα-N bond torsion for Pro1 in the acyclic precursor, through its substitution for a D-Ala residue, effectively decouples the motion of the second carboxamide group from the Cα-N bond torsion and allows the second carboxamide group to rotate. This rotation allows a helical conformation to develop in the transition state to the macrocycle without the need to align all of the carboxamide dipoles and results in successful cyclization to give template structures of the all trans (ttt) form. Deriva. of the template were prepared by extending the C-terminus and these were characterized by NMR and restrained

L4 ANSWER 187 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
simulated annealing. In CDCl3 soln. at low temp., sep. sets of NMR signals were obsd. for two rapidly interconverting helical conformational isomers of the thioether macrocycle I which possessed an appended trialkylammonium ion. The free energy of activation for the transition (ΔGc.dbldag.) was 48 kJ mol-1. A similar time-averaged conformation was also obsd. in aq. soln. At -80° in dichloromethane the rate of conformational exchange was slowed sufficiently to obtain resonance assignments and NOE data sep. for each isomer. In the minor isomer (40%), the four carbonyl oxygen hydrogen-bond acceptors of the template are aligned in an α-helical conformation and in the major conformer the Pro2 carbonyl dipole was anti-aligned with the other three dipoles. Thus, the conformers differ in the orientation of one carbonyl group. Mol. modeling calcns. showed that the minor isomer was stabilized by coulombic interactions between the trialkylammonium salt and the carbonyl group dipole moments.
IT **220061-81-4P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation) (design, construction, and properties of proline-containing cyclotetrapeptide N-terminal cap templates devised to initiate α-helixes)
RN 220061-81-4 CAPLUS
CN L-Phenylalaninamide, 1-[(2S)-2-mercapto-1-oxopropyl]-L-prolyl-D-alanyl-(4S)-4-mercapto-L-prolyl-N-methyl-, cyclic (1→3)-thioether (9CI) (CA INDEX NAME)

Absolute stereochemistry.



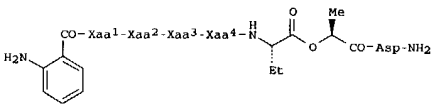
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 188 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:708845 CAPLUS
DOCUMENT NUMBER: 129:316563
TITLE: Preparation of peptide amides and depsipeptide amides as hepatitis C NS3 protease inhibitors
INVENTOR(S): Hart, Terance; Quibell, Martin
PATENT ASSIGNEE(S): Peptide Therapeutics Ltd., UK
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9846630	A1	19981022	WO 1998-GB1126	19980416
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9870635	A1	19981111	AU 1998-70635	19980416
EP 975662	A1	20000202	EP 1998-917395	19980416
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001521516	T2	20011106	JP 1998-543648	19980416

PRIORITY APPLN. INFO.: GB 1997-7659 A 19970416
WO 1998-GB1126 W 19980416

GI

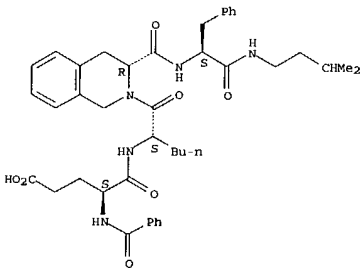


I

AB Disclosed is a specific pharmacophoric profile which represents the structure for inhibitors of hepatitis C NS3 protease. The results from mapping studies of the enzyme with depsipeptide substrates I (Xaa1 = Glu, D-Glu, Gln, Val, 2-aminobutyryl; Xaa2 = Nle, Glu, Val, Tyr; Xaa3 = Glu, Val, Ser, Nle, 3-pyridylalanyl, homophenylalanyl, Tyr; Xaa4 = Glu, Leu, Phe, Pro) allow the generation of a particular pharmacophoric binding profile. Peptide amides Bz-Glu-Nle-Xaa5-Xaa6-NHR [Xaa5 = D-1,2,3,4-tetrahydroquinoline-3-carboxylic acid (D-Tic), homophenylalanine; Xaa6 = Leu, Phe, Glu; R = CH2CH2CHMe2, CH2CH2Ph, n-Pr] possessing this motif were shown to be inhibitors of hepatitis NS3 protease. The inhibitors have use in the treatment of hepatitis C.
IT **214910-67-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

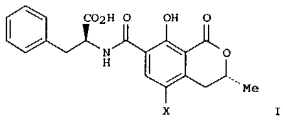
L4 ANSWER 188 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of peptide amides as hepatitis C NS3 protease inhibitors)
RN 214910-67-5 CAPLUS
CN L-Phenylalaninamide, N-benzoyl-L-α-glutamyl-L-norleucyl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-N-(3-methylbutyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 189 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:680190 CAPLUS
DOCUMENT NUMBER: 130:34337
TITLE: On the role of copper and iron in DNA cleavage by ochratoxin A. Structure-activity relationships in metal binding and copper-mediated DNA cleavage
AUTHOR(S): Ardus, Jason A.; Gillman, Ivan G.; Manderville, Richard A.
CORPORATE SOURCE: Department of Chemistry, Wake Forest University, Winston-Salem, NC, 27109-7486, USA
SOURCE: Canadian Journal of Chemistry (1998), 76(6), 907-918
CODEN: CJCHAG; ISSN: 0008-4042
PUBLISHER: National Research Council of Canada
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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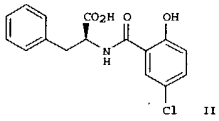


II

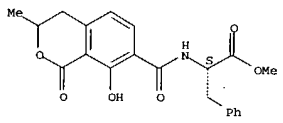
AB Ochratoxin A (OTA, I: X = Cl) is a fungal carcinogen that facilitates single-strand DNA cleavage and DNA adduction when metabolically activated. To determine if redox-active transition metals induce OTA-mediated DNA damage, we have examined the toxin's ability to bind Cu(II) and Fe(III) in aqueous media and facilitate DNA cleavage in their presence using agarose gel electrophoresis and supercoiled plasmid DNA. Using fluorescence spectroscopy, I was found to bind Cu(II) readily at physiol. pH, while acidic conditions (pH 2.6) were employed to study Fe(III) binding due to the formation of Fe-oxide ppts. at higher pH values. Structure-activity relationships employing synthetic derivs. of I implied that I binds both Cu(II) and Fe(III) by its phenolic oxygen, while the carboxylic acid of its phenylalanine moiety binds Cu(II), but does not appear to play a role in Fe(III) coordination at pH 2.6. In terms of metal-mediated DNA cleavage, no role for I could be detected in Fe-induced DNA strand

L4 ANSWER 189 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

scission. With Cu(II), DNA cleavage by the 1:1 copper-bound complex of I could only be initiated by addn. of a suitable reducing agent (sodium ascorbate). However, I was found to facilitate DNA cleavage by the Cu(II) complex of 1,10-phenanthroline (Cu(OP)2); a prototypical Cu-mediated nuclease system that cleaves DNA upon activation by an external reducing agent. Structure-activity relationships employing analogs lacking the chlorine atom, ochratoxin B, I: X = H, and the lactone (II), indicated that the chlorine atom is essential for activity of the OTA in potentiating DNA cleavage by Cu(OP)2. The implications of our findings to the genotoxic properties of I are discussed.

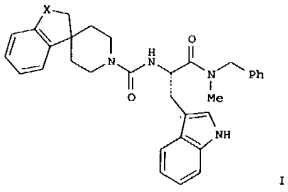
IT **216967-81-6P**
RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and hydrolysis)
RN 216967-81-6 CAPLUS
CN L-Phenylalanine, N-[(3,4-dihydro-8-hydroxy-3-methyl-1-oxo-1H-2-benzopyran-7-yl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 57 THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 190 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:606905 CAPLUS
DOCUMENT NUMBER: 129:290398
TITLE: LTryptophan urea amides as NK1/NK2 dual antagonists
AUTHOR(S): Qi, Hongbo; Shah, Shrenik K.; Cascieri, Margaret A.; Sadowski, Sharon J.; MaCcoss, Malcolm
CORPORATE SOURCE: Department of Medicinal Chemistry and Department of Molecular Pharmacology and Biochemistry, Rahway, NJ, 07065, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(16), 2259-2262
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



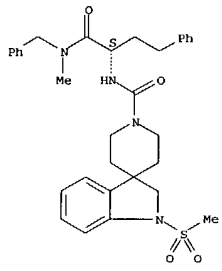
I

AB The authors report that a systematic modification of an NK1 receptor selective antagonist resulted in the identification of novel compds. I (X = CH2, NSO2Me) with high affinity for both NK1 and NK2 receptors.

IT **199110-44-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and neurokinin receptor dual antagonist activity of substituted tryptophan amides)
RN 199110-44-6 CAPLUS
CN Spiro[3H-indole-3,4'-piperidine]-1'-carboxamide, 1,2-dihydro-N-[(1S)-1-[[methyl(phenylmethyl)amino]carbonyl]-3-phenylpropyl]-1-(methylsulfonyl)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

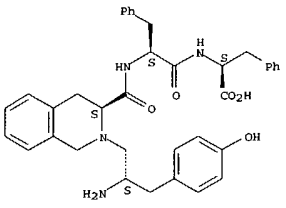
L4 ANSWER 190 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 191 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:597984 CAPLUS
DOCUMENT NUMBER: 130:10306
TITLE: The receptor-bound conformation of H-Tyr-Tic-(Phe-Phe)-OH related δ-opioid antagonists contains all trans peptide bonds
AUTHOR(S): Wilkes, B. C.; Nguyen, T. M-D.; Weltrowska, G.; Carpenter, K. A.; Lemieux, C.; Chung, N. N.; Schiller, P. W.
CORPORATE SOURCE: Laboratory of Chemical Biology and Peptide Research, Clinical Research Institute of Montreal, Montreal, QC, H2W 1R7, Can.
SOURCE: Peptides 1996, Proceedings of the European Peptide Symposium, 24th, Edinburgh, Sept. 8-13, 1996 (1998), Meeting Date 1996, 911-912. Editor(s): Ramage, Robert; Epton, Roger. Mayflower Scientific: Kingswinford, UK.
CODEN: 66RCA5
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A mol. mechanics study and energy minimization of two peptide δ-opioid antagonists containing a tetrahydroisoquinoline-3-carboxylic acid (Tic) residue revealed low energy conformers consistent with the previously proposed receptor-bound conformation containing all trans peptide bonds. No conformations with cis peptide bonds were found for either peptide. Assuming that all compds. of Tic-containing peptides have similar conformational requirements for δ-antagonism, their bioactive conformations must contain all trans peptide bonds.
IT **207342-54-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(receptor-bound conformation of H-Tyr-Tic-(Phe-Phe)-OH related δ-opioid antagonists contains all trans peptide bonds)
RN 207342-54-9 CAPLUS
CN L-Phenylalanine, (3S)-2-[(2S)-2-amino-3-(4-hydroxyphenyl)propyl]-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



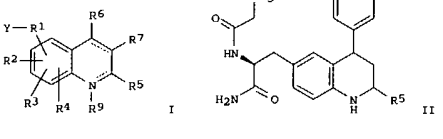
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 191 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L4 ANSWER 192 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:543220 CAPLUS
DOCUMENT NUMBER: 129:175563
TITLE: 4-Substituted quinoline derivatives and 4-substituted quinoline combinatorial libraries
INVENTOR(S): Hayes, Thomas K.; Forood, Behrouz; Kiely, John S.
PATENT ASSIGNEE(S): Trega Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

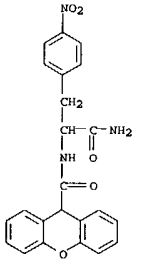
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9834115	A1	19980806	WO 1997-US22391	19971205
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9881919	A1	19980825	AU 1998-81919	19971205
EP 977989	A1	20000209	EP 1997-949775	19971205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 6262269	B1	20010717	US 1998-17785	19980203
US 6388081	B1	20020514	US 1999-376670	19990816

PRIORITY APPLN. INFO.: US 1997-795392 A 19970204
US 1997-126414P P 19970204
WO 1997-US22391 W 19971205
US 1998-17785 A3 19980203
OTHER SOURCE(S): MARPAT 129:175563
GI



AB The invention relates to novel 4-substituted quinoline derivs. I, their salts, and combinatorial libraries containing mixts. of two or more such compds. [wherein R1 = bond, (un)substituted alk(en/yn)ylene, cycloalk(en)ylene, phenylene, naphthylene, heterocycle, heteroaryl, amino, CH2CONH, (CH2)pAr(CH2)q, etc.; p, q = 0-6 but both cannot be 0; Ar =

L4 ANSWER 192 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(un)substituted Ph or heteroaryl; R2, R3, R4 = H, halo, (un)protected OH, cyano, NO2, (un)substituted alk(en/yn)yl, alkoxy, cycloalk(en)yl, heterocyclyl, phenylalkyl, Ph, naphthyl, etc.; R5 = H, (un)substituted alk(en/yn)yl, cycloalk(en)yl, Ph, naphthyl, phenylalkyl, (un)protected CO2H, acyl, heterocyclyl, etc.; R6 = H, (un)substituted Ph, naphthyl, 2-oxopyrrolidin-1-yl and higher homologs, (un)substituted NHCHO; R7 = H, (un)substituted alkyl; Y = CO2H, OH, SH, NHR8, CONHR8, CH2OH, CH2NH2, CH2NHR8; R8 = H, (un)substituted alkyl, or functionalized resin; R9 = H, (un)substituted alkyl, phenylalkyl, acyl, PhSO2, alkylsulfonyl, alkylaminocarbonyl, or PhNHCO, or is absent; dotted lines = optional pi bonds]. The invention also relates to the generation of such libraries. In 12 examples, libraries of I ranging in size from 2380 to 39,440 compds. were prepd. as mixed sublibraries. Data for control compds. (samples of individually known intermediates and products, cleaved from simultaneously processed control resins) are given for some examples. Both quinoline and tetrahydroquinoline libraries were prepd. For instance, tea-bags of MBHA resin were each coupled with L- or D-N-BOC-p-nitrophenylalanine, the BOC groups were removed from both, and the amino groups were each acylated with 170 carboxylic acids. The acylated, resin-bound products were mixed and reduced at the nitro group, and the amine product mixts. were condensed with 58 different aldehydes and cyclized with 4-methoxystyrene. Cleavage of the resin-bound products with HF gave mixed sublibraries of I. Individual control samples of products, such as II [R5 = 1-naphthyl, 2,3-difluorophenyl, cyclohexyl, etc.], were obtained by reactions of pure, resin-bound L-N-propanoyl-p-aminophenylalanine control samples with individual aldehydes and 4-methoxystyrene. Potential applications of I (no data) may include use as antibacterials, NMDA antagonists, or analgesics.
IT **211376-13-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(resin-cleavage control intermediate; preparation of tricyclic tetrahydroquinoline derivs. and combinatorial libraries)
RN 211376-13-5 CAPLUS
CN 9H-Xanthene-9-carboxamide, N-[2-amino-1-[(4-nitrophenyl)methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

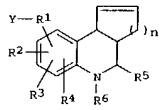
L4 ANSWER 192 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L4 ANSWER 193 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:543216 CAPLUS
DOCUMENT NUMBER: 129:175562
TITLE: Tricyclic tetrahydroquinoline derivatives and tricyclic tetrahydroquinoline combinatorial libraries
INVENTOR(S): Hayes, Thomas K.; Kiely, John S.
PATENT ASSIGNEE(S): Trega Biosciences, Inc., USA
SOURCE: PCT Int. Appl., 119 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9834111	A1	19980806	WO 1997-US22206	19971205
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5925527	A	19990720	US 1997-795893	19970204
AU 9855928	A1	19980825	AU 1998-55928	19971205
NZ 337046	A	20000128	NZ 1997-337046	19971205
EP 983507	A1	20000308	EP 1997-952280	19971205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-795893 A 19970204
WO 1997-US22206 W 19971205
OTHER SOURCE(S): MARPAT 129:175562
GI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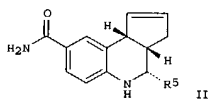

II

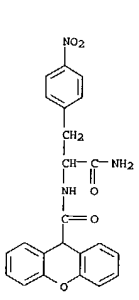
AB The invention relates to novel tricyclic tetrahydroquinoline compds. I, their salts, and combinatorial libraries containing mixts. of two or more such compds. [wherein R1 = bond, (un)substituted alk(en/yn)ylene, cycloalk(en)ylene, phenylene, naphthylene, heterocycle, heteroaryl, amino, CH2CONH, (CH2)pAr(CH2)q; p, q = 0-6 but both cannot be 0; Ar = (un)substituted Ph or heteroaryl; R2, R3, R4 = H, halo, (un)protected OH, cyano, NO2, (un)substituted alk(en/yn)yl, alkoxy, cycloalk(en)yl, heterocyclyl, phenylalkyl, Ph, naphthyl, etc.; R5 = H, (un)substituted alk(en/yn)yl, cycloalk(en)yl, Ph, naphthyl, phenylalkyl, (un)protected CO2H, acyl, heterocyclyl, etc.; R6 = H, (un)substituted alkyl,

L4 ANSWER 193 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

phenylalkyl, acyl, PhSO2, alkylsulfonyl, alkylaminocarbonyl, PhNHCO; n = 1-3; Y = CO2H, OH, SH, NHR7, CONHR7, CH2OH, CH2NH2, CH2NHR7; R7 = H, (un)substituted alkyl, or functionalized resin; R1 must be present and R5 = Ph when Y = CO2H]. The invention also relates to the generation of such libraries. In 2 examples, libraries of 2774 and approx. 17,000 compds. I were prepd. as mixed sublibraries. Data for control compds. (samples of individually known intermediates and products, cleaved from simultaneously processed control resins) are given. For instance, tea-bags of MBHA resin were each coupled with one of 19 aminobenzoic acids, such as 4-aminobenzoic acid. Diagnostic cleavage of each of these resins with HF gave 19 aminobenzamide controls in 34-99% yield. The 19 resins were mixed together and placed in new tea-bags, then condensed with 73 different aldehydes, and finally cyclized with cyclopentadiene. Cleavage of the resin-bound products with HF gave approx. 73 mixts. of 38 compds. (counting sep. enantiomers). Individual control samples of products, such as II [R5 = H, CH2Cl, cyclohexyl, CO2H, (un)substituted Ph, etc.], were typically obtained in 50-100% yield by reactions of pure, resin-bound 4-aminobenzoic acid control samples in sibling tea-bags. Potential applications of I (no data) may include use as antibacterials or analgesics.

IT **211376-13-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(resin-cleavage control intermediate; preparation of tricyclic tetrahydroquinoline derivs. and combinatorial libraries)

RN 211376-13-5 CAPLUS
CN 9H-Xanthene-9-carboxamide, N-[2-amino-1-[(4-nitrophenyl)methyl]-2-oxoethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 194 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

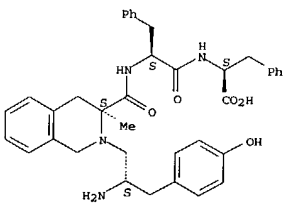
ACCESSION NUMBER: 1998:507698 CAPLUS
DOCUMENT NUMBER: 129:245476
TITLE: Conformationally constrained opioid peptide analogs with novel activity profiles
AUTHOR(S): Schiller, Peter W.; Schmidt, Ralf; Weltrowska, Grazyna; Berezowska, Irena; Nguyen, Thi M.-D.; Dupuis, Sebastien; Chung, Nga N.; Lemieux, Carole; Wilkes, Brian C.; Carpenter, Katharine A.
CORPORATE SOURCE: Laboratory of Chemical Biology and Peptide Research, Clinical Research Institute of Montreal, Montreal, QC, H2W 1R7, Can.
SOURCE: Letters in Peptide Science (1998), 5(2-3), 209-214
CODEN: LPSCEM; ISSN: 0929-5666
PUBLISHER: Kluwer Academic Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Novel conformationally constrained opioid peptide analogs, having properties as δ antagonist, mixed μ agonist/δ antagonist or δ agonist, were developed. TIP(P)-related δ antagonists showed unprecedented δ antagonist potency and δ receptor selectivity, and may have potential for use in analgesia in combination with μ agonists. A definitive model of their δ receptor-bound conformation was developed. Three prototype mixed μ agonist/δ antagonists were discovered. They represent the only known compds. with this pharmacol. profile and, as expected, one of them was shown to be a potent analgesic and to produce no dependence and less tolerance than morphine. Novel dipeptide derivs. turned out to be potent and selective δ agonists. Because of their low mol. weight and lipophilic character, these compds. may cross the blood-brain barrier and, thus, may have potential as centrally acting analgesics.

IT **207342-55-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(activity profiles of conformationally constrained opioid peptide analogs)

RN 207342-55-0 CAPLUS
CN L-Phenylalanine, (3S)-2-[(2S)-2-amino-3-(4-hydroxyphenyl)propyl]-1,2,3,4-tetrahydro-3-methyl-3-isoquinolinecarbonyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 194 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L4 ANSWER 195 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:479021 CAPLUS
DOCUMENT NUMBER: 129:122868
TITLE: Preparation of peptidylboronic ester and acid compounds as proteasome inhibitors
INVENTOR(S): Adams, Julian; Ma, Yu-Ting; Stein, Ross; Baevsky, Matthew; Grenier, Louis; Plamondon, Louis
PATENT ASSIGNEE(S): Proscript, Inc., USA
SOURCE: U.S., 37 pp., Cont.-in-part of U.S. Ser. No. 442,581.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5780454	A	19980714	US 1995-549318	19951027
US 6083903	A	20000704	US 1995-442581	19950516
US 6066730	A	20000523	US 1998-85404	19980526
US 6297217	B1	20011002	US 2000-490511	20000125
US 6465433	B1	20021015	US 2001-953540	20010914
US 2002173488	A1	20021121	US 2002-100295	20020318
US 6548668	B2	20030415		
US 6617317	B1	20030909	US 2002-125997	20020419
US 2003199561	A1	20031023	US 2003-392165	20030319

PRIORITY APPLN. INFO.:
US 1994-330525 B2 19941028
US 1995-442581 A2 19950516
US 1995-549318 A3 19951027
US 1998-85404 A3 19980526
US 2000-490511 A1 20000125
US 2001-953540 A1 20010914
US 2002-100295 A1 20020318
US 2002-125997 A1 20020419

OTHER SOURCE(S): MARPAT 129:122868
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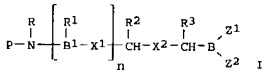
L4 ANSWER 195 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



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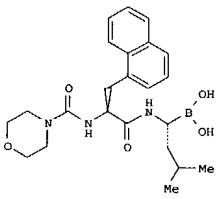

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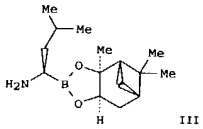


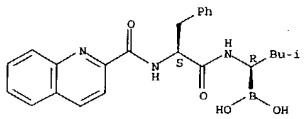
III

AB Disclosed herein is a method for reducing the rate of degradation of proteins in an animal comprising contacting cells of the animal with certain boronic ester and acid compds I [P = aryl-, aralkyl-, heteroaryl-, or heteroarylalkylcarbonyl or -sulfonyl; B1 = N, CH; X1, X2 = CONH, CH(OH)CH2, COCH2; n = 0, 1, 2; R = H, alkyl; RR1 or RR2 (for n = 0) may form a ring; R1, R2, R3 = H, alkyl, cycloalkyl, aryl, etc.; Z1, Z2 = alkyl, hydroxy, alkoxy, aryloxy; Z1Z2 may form a moiety derived from a dihydroxy compound]. Also disclosed herein are novel boronic ester and acid compds., their synthesis and uses. Thus, peptidylboronic acid II was prepared by coupling pinanediol leucine boronate ester III with N-Boc-β-(1-naphthyl)-L-alanine, followed by deprotection, acylation with 4-morpholinecarbonyl chloride, and cleavage of the pinanediol moiety. II inhibited proteasome 20S with Ki = 0.18 nM.

IT **179324-53-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptidylboronic ester and acid compds. as proteasome inhibitors)

RN 179324-53-9 CAPLUS
CN Boronic acid, [(1R)-3-methyl-1-[[(2S)-1-oxo-3-phenyl-2-[(2-quinolinylcarbonyl)amino]propyl]amino]butyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS

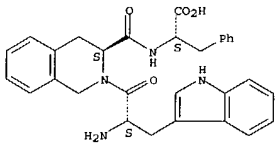
L4 ANSWER 195 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 196 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:427361 CAPLUS
DOCUMENT NUMBER: 129:156465
TITLE: A potent dipeptide inhibitor of dipeptidyl peptidase IV
AUTHOR(S): Yamada, Masaki; Okagaki, Chieko; Higashijima, Takanori; Tanaka, Sumiko; Ohnuki, Tetsuo; Sugita, Takahisa
CORPORATE SOURCE: Lead Generation Research Laboratory, Tanabe Seiyaku Co., Ltd., Osaka, 532-8505, Japan
SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(12), 1537-1540
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of novel potent inhibitors of dipeptidyl peptidase IV (DPP-IV) has been developed. A brief structure-activity relation of the inhibitors was investigated. The dipeptide TSL-225, tryptophyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid, was identified with the critical structure for the inhibitory activity.

IT **207228-59-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of potent dipeptide inhibitors of dipeptidyl peptidase IV in relation to structure)
RN 207228-59-9 CAPLUS
CN L-Phenylalanine, L-tryptophyl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

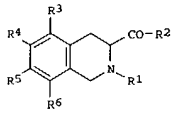


REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 197 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:293475 CAPLUS
DOCUMENT NUMBER: 129:4862
TITLE: Preparation of amino acid-containing tetrahydroisoquinoline derivatives as dipeptidyl peptidase IV inhibitors
INVENTOR(S): Sugita, Takahisa; Ohnuki, Tetsuo; Yamada, Masaki; Tanaka, Sumiko; Nonaka, Nobuaki; Asai, Yasuyuki
PATENT ASSIGNEE(S): Tanabe Seiyaku Co., Ltd., Japan; Sugita, Takahisa; Ohnuki, Tetsuo; Yamada, Masaki; Tanaka, Sumiko; Nonaka, Nobuaki; Asai, Yasuyuki
SOURCE: PCT Int. Appl., 87 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9818763	A1	19980507	WO 1997-JP3804	19971022
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
JP 10182613	A2	19980707	JP 1997-288322	19971021
AU 9747218	A1	19980522	AU 1997-47218	19971022
PRIORITY APPLN. INFO.:			JP 1996-284328	19961025
			WO 1997-JP3804	19971022

OTHER SOURCE(S): MARPAT 129:4862
GI



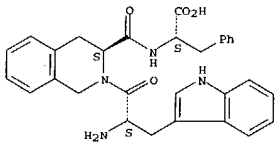
I

AB The title compds. I [R1 = amino protecting group, etc.; R2 = optionally protected hydroxy, etc.; R3 - R6 = H, hydroxy, alkoxy] are prepared In an in vitro test, 21 compds. of this invention showed inhibiting activity against dipeptidyl peptidase IV. (3S)-2-(L-Tryptophyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid hydrochloride at 30 mg/kg/day s.c. for 18 days gave significant inhibition of exptl. arthritis in rats.

IT **207228-59-9P**

L4 ANSWER 197 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of amino acid-contg. tetrahydroisoquinoline derivs. as dipeptidyl peptidase IV inhibitors)
RN 207228-59-9 CAPLUS
CN L-Phenylalanine, L-tryptophyl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



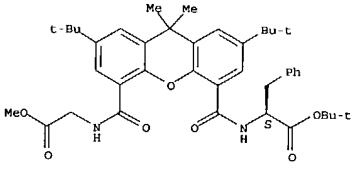
REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 198 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:277671 CAPLUS
DOCUMENT NUMBER: 128:289517
TITLE: Rapid characterization of combinatorial libraries using electrospray ionization Fourier transform ion cyclotron resonance mass spectrometry
AUTHOR(S): Fang, A. S.; Vouros, P.; Stacey, C. C.; Kruppa, G. H.; Laukien, F. H.; Wintner, E. A.; Carell, T.; Rebek, J., Jr.
CORPORATE SOURCE: Department of Chemistry, Barnett Institute, Northeastern University, Boston, MA, 02115, USA
SOURCE: Combinatorial Chemistry and High Throughput Screening (1998), 1(1), 23-33
CODEN: CCHSFU; ISSN: 1386-2073
PUBLISHER: Bentham Science Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The relatively new field of combinatorial chemical has enabled researchers to create large mixts. of compds. that can be screened for leads in developing potential drug candidates. The new synthetic method has also created a need for better procedures to analyze the complex mixts. that are generated. The immediate goal in most cases is to verify the synthetic procedure and to determine the purity and completeness of the library sample before binding studies are initiated. The authors report here a method to rapidly characterize small-mol. combining a core mol. bearing two acid chloride functionalities with various amino acids to generate libraries of 36, 78 and 120 components. Using electrospray ionization Fourier transform ICR mass spectrometry (ESI-FTICR-MS) the authors were able to identify 70-80% of the library components. All samples were analyzed as mixts. by direct infusion without chromatog. separation Also, nominally isobaric components could be resolved and identified through exact mass assignments without tandem mass spectrometry. ESI-FTICR-MS is a rapid and convenient tool for the characterization of small-mol. libraries. The method is especially useful for the anal. of larger libraries that contain many nominally isobaric components and impurities.

IT **178916-07-9**
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(rapid characterization of combinatorial libraries using electrospray ionization Fourier transform ion cyclotron resonance mass spectrometry)
RN 178916-07-9 CAPLUS
CN L-Phenylalanine, N-[[2,7-bis(1,1-dimethylethyl)-5-[[(2-methoxy-2-oxoethyl)amino]carbonyl]-9,9-dimethyl-9H-xanthen-4-yl]carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

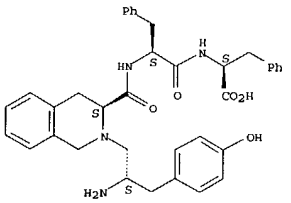
Absolute stereochemistry.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS

L4 ANSWER 198 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 199 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 199 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:265652 CAPLUS
DOCUMENT NUMBER: 129:4851
TITLE: The receptor-bound conformation of H-Tyr-Tic-(Phe-Phe)-OH-related δ-opioid antagonists contains all trans peptide bonds
AUTHOR(S): Wilkes, Brian C.; Nguyen, Thi M. -D.; Weltrowska, Grazyna; Carpenter, Katharine A.; Lemieux, Carole; Chung, Nga N.; Schiller, Peter W.
CORPORATE SOURCE: Laboratory of Chemical Biology and Peptide Research, Clinical Research Institute of Montreal, Montreal, QC, H2W 1R7, Can.
SOURCE: Journal of Peptide Research (1998), 51(5), 386-394
CODEN: JPERFA; ISSN: 1397-002X
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Two different models for the receptor-bound conformation of δ-opioid peptide antagonists containing the N-terminal dipeptide segment "Tyr-Tic" (Tic = 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid) have been proposed. Both models are based on spatial overlap of the Tyr1 and Tic2 aromatic rings and N-terminal amino group with the corresponding aromatic rings and nitrogen atom of the nonpeptide δ-antagonist naltrindole. However, in one model the peptide bond between the Tyr1 and Tic2 residues assumes the trans conformation, whereas in the other it is in the cis conformation. To distinguish between these two models, the authors prepared the two peptides H-Tyrψ[CH2NH]Tic-Phe-Phe-OH and H-Tyrψ[CH2NH]MeTic-Phe-Phe-OH (MeTic = 3-methyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid) in which a cis peptide bond between the Tyr and Tic (or MeTic) residues is sterically forbidden. Both compds. turned out to be moderately potent δ-opioid antagonists in the mouse vas deferens assay. A mol. mechanics study performed with both peptides resulted in low-energy conformations in which the torsional angle ("ω1") of the reduced peptide bond between Tyr and Tic (or MeTic) had a value of 180° (trans conformation) and which were in good agreement with the proposed model with all trans peptide bonds. Also, this study confirmed that neither of these two peptides could assume low-energy conformations in which "ω1" had a value of 0° (cis conformation). Conformers with that same bond in the gauche conformation ("ω1" = -60°) were also identified, but were higher in energy and showed no spatial overlap with naltrindole. Thus, it is concluded that the receptor-bound conformation of δ-peptide antagonists containing an N-terminal "Tyr-Tic" dipeptide segment must have all trans peptide bonds.

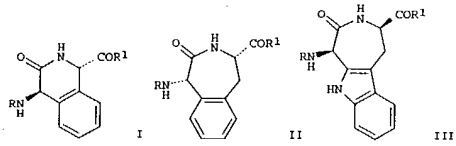
IT **207342-54-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(conformation study of the receptor bound "Tyr-Tic" peptide segment of δ-opioid antagonists)

RN 207342-54-9 CAPLUS
CN L-Phenylalanine, (3S)-2-[(2S)-2-amino-3-(4-hydroxyphenyl)propyl]-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 200 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1998:265646 CAPLUS
DOCUMENT NUMBER: 129:4850
TITLE: Synthesis of cyclic dipeptide templates, their incorporation into peptides and studies on their conformational and biological properties
AUTHOR(S): Asche, Geert; Kunz, Horst; Nar, Herbert; Koppen, Herbert; Briem, Hans; Pook, Karl-Heinz; Schiller, Peter W.; Chung, Nga N.; Lemieux, Carole; Esser, Franz
CORPORATE SOURCE: Departments of Medicinal Chemistry and Analytical Sciences, Boehringer Ingelheim, Ingelheim, Germany
SOURCE: Journal of Peptide Research (1998), 51(5), 323-336
CODEN: JPERFA; ISSN: 1397-002X
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I II III

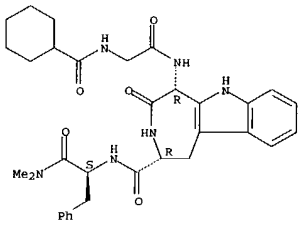
AB This study investigated the diastereoselective synthesis of three dipeptide templates I-III [R = Cl3CCH2O2C, PhCH2O2C (Cbz); R1 = OH], which may be regarded as conformationally restricted analogs of H-Gly-Xaa-OH, in which Xaa constitutes an aromatic amino acid. Bond formation between α-C of Gly and the aromatic moiety was achieved by proton-catalyzed intramol. electrophilic aromatic substitution. The absolute configuration of the dipeptide templates was determined by single-crystal x-ray crystallog. or by NOE measurements. A protective group strategy was elaborated to allow their incorporation into peptide sequences by liquid phase as well as by solid-phase peptide synthesis. The templates were used to generate enkephalin analog II (R = H-Tyr-Gly, R1 = Leu-NH2), modified neurokinin antagonist III (R = N-cyclohexylcarbonylglycyl, R1 = Phe-NMe2) and dermorphin derivs. I and II (R = H-Tyr-D-Ala, Phe; R1 = Pro-Ser-NH2). Mol. dynamic simulations of enkephalin analog II (R = H-Tyr-Gly, R1 = Leu-NH2) and neurokinin antagonist III (R = N-cyclohexylcarbonylglycyl, R1 = Phe-NMe2) revealed the preference for a turn-like motif for the enkephalin analog. The biol. activity, as investigated by resp. receptor binding and functional assays, was strongly diminished with all four derivs., indicating that their receptor-relevant mol. geometries lie outside the examined conformational space.

IT **207443-93-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, conformation, and receptor-binding of conformationally constrained aromatic dipeptide template-containing peptides)

RN 207443-93-4 CAPLUS
CN Azepino[4,5-b]indole-2-carboxamide, 5-[[[(cyclohexylcarbonyl)amino]acetyl]

L4 ANSWER 200 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
amino]-N-[(1S)-2-(dimethylamino)-2-oxo-1-(phenylmethyl)ethyl]-1,2,3,4,5,6-hexahydro-4-oxo-, (2R,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



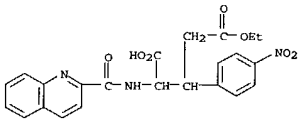
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 201 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:233609 CAPLUS
DOCUMENT NUMBER: 128:295021
TITLE: Solid-phase synthesis of substituted glutamic acid derivatives via Michael addition reactions
AUTHOR(S): Dominguez, Esteban; O'donnell, Martin J.; Scott, William L.
CORPORATE SOURCE: Centro de Investigacion Lilly, Madrid, 28130, Spain
SOURCE: Tetrahedron Letters (1998), 39(15), 2167-2170
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The conjugate addition of Michael acceptors to the resin-bound benzophenone imine of glycine, Ph2C:NCH2CO2-Resin (I), leads to a variety of racemic unnatural glutamic acid deriva. This new approach expands the scope of unnatural amino acid and peptide synthesis. For example, RCONHCH(CO2H)CH(C6H4NO2-4)CH2CO2Et (R = 2-quinolinyl) was synthesized in 88% yield from I, EtO2CCH:CHC6H4NO2-4 and quinaldic acid.

IT **206070-97-5P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid-phase synthesis of substituted glutamic acids via Michael addition reactions)

RN 206070-97-5 CAPLUS
CN Glutamic acid, 3-(4-nitrophenyl)-N-(2-quinolinylcarbonyl)-, 5-ethyl ester (9CI) (CA INDEX NAME)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

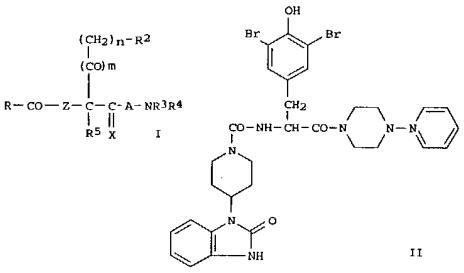
L4 ANSWER 202 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:197358 CAPLUS
DOCUMENT NUMBER: 128:257695
TITLE: Preparation of modified amino acids and their use as calcitonin gene-related peptide antagonists in pharmaceutical compositions
INVENTOR(S): Rudolf, Klaus; Eberlein, Wolfgang; Engel, Wolfhard; Pieper, Helmut; Doods, Henri; Hallermayer, Gerhard; Entzeroth, Michael; Wienen, Wolfgang
PATENT ASSIGNEE(S): Karl Thomae G.m.b.H., Germany
SOURCE: PCT Int. Appl., 461 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9811128	A1	19980319	WO 1997-EP4862	19970908
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
DE 19636623	A1	19980312	DE 1996-19636623	19960910
DE 19720011	A1	19981119	DE 1997-19720011	19970514
AU 9741196	A1	19980402	AU 1997-41196	19970908
AU 721035	B2	20000622		
EP 927192	A1	19990707	EP 1997-938928	19970908
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9712023	A	19990831	BR 1997-12023	19970908
JP 2000505100	T2	20000425	JP 1998-513227	19970908
JP 3483893	B2	20040106		
NO 9901130	A	19990505	NO 1999-1130	19990309
KR 2000044040	A	20000715	KR 1999-702008	19990310
US 6344449	B1	20020205	US 1999-254281	19991012
US 2001036946	A1	20011101	US 2001-789391	20010221
US 2003069231	A1	20030410	US 2002-119875	20020410

PRIORITY APPLN. INFO.: DE 1996-19636623 A 19960910
DE 1997-19720011 A 19970514
WO 1997-EP4862 W 19970908
US 1999-254281 A1 19991012
US 2001-789391 A1 20010221

OTHER SOURCE(S): MARPAT 128:257695
GI

L4 ANSWER 202 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



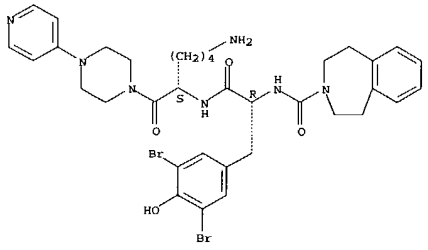
AB The invention concerns modified amino acids of general formula I [A = bond, CX; Z = CH2, NR1; R1 = H, alkyl, phenyl-alkyl; X = O, H,H; n = 1-2; m = 0-1; R = (substituted)alkyl; R2 = Ph, (substituted)(hetero)(bi)cycle; R3 = H, (substituted)alkyl, Ph, pyridinyl; R4 = H, (substituted)alkyl; R3R4= (hetero)cycle; R5 = H, alkyl, alkoxycarbonyl, PhCH2], pharmaceuticals containing these compds., their use and the method for their production, as well as their use for the production and purification of antibodies and as marked compds. in RIA and ELISA assays and as diagnostic or analytic auxiliary agents in neurotransmitter research. Thus, 3,5-dibromo-N2-[4-(1,3-dihydro-2(2H)-oxo-benzimidazol-1-yl)-1-piperidinyl]carbonyl-D-tyrosine was reacted with 1-(4-pyridinyl)-piperazine, to give II(22%). Title compds. show human calcitonin gene related peptide (CGRP) antagonist activity; in in-vitro binding studies with Sk-N-MC-cells, I had IC50 ≤10000 nM, and in the same system, had CGRP-antagonist activity at doses from 10-11 to 10-6 M.

IT **204698-94-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acids and their use as calcitonin gene-related peptide antagonists in pharmaceutical compns.)

RN 204698-94-2 CAPLUS
CN 3H-3-Benzazepine-3-carboxamide, N-[2-[[5-amino-1-[[4-(4-pyridinyl)-1-piperazinyl]carbonyl]pentyl]amino]-1-[(3,5-dibromo-4-hydroxyphenyl)methyl]-2-oxoethyl]-1,2,4,5-tetrahydro-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 202 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 203 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

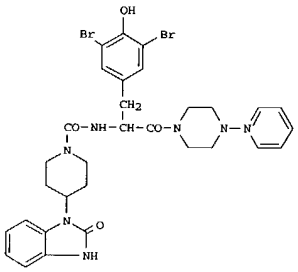
ACCESSION NUMBER: 1998:186625 CAPLUS
DOCUMENT NUMBER: 128:230701
TITLE: Preparation of varied amino acids as calcitonin gene-related peptide antagonists in pharmaceutical compositions
INVENTOR(S): Rudolf, Klaus; Eberlein, Wolfgang; Engel, Wolfhard; Pieper, Helmut; Doods, Henri; Hallermayer, Gerhard; Entzeroth, Michael; Wienen, Wolfgang
PATENT ASSIGNEE(S): Karl Thomae G.m.b.H., Germany
SOURCE: Ger. Offen., 142 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19636623	A1	19980312	DE 1996-19636623	19960910
WO 9811128	A1	19980319	WO 1997-EP4862	19970908
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9741196	A1	19980402	AU 1997-41196	19970908
AU 721035	B2	20000622		
EP 927192	A1	19990707	EP 1997-938928	19970908
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9712023	A	19990831	BR 1997-12023	19970908
CN 1230196	A	19990929	CN 1997-197772	19970908
CN 1129605	B	20031203		
JP 2000505100	T2	20000425	JP 1998-513227	19970908
JP 3483893	B2	20040106		
JP 2003300959	A2	20031021	JP 2003-21750	19970908
ZA 9708083	A	19991217	ZA 1997-8083	19970909
TW 477792	B	20020301	TW 1997-86113120	19970910
TW 498076	B	20020811	TW 2000-89125839	19970910
NO 9901130	A	19990505	NO 1999-1130	19990309
US 6344449	B1	20020205	US 1999-254281	19991012

PRIORITY APPLN. INFO.: DE 1996-19636623 A 19960910
DE 1997-19720011 A 19970514
JP 1998-513227 A3 19970908
WO 1997-EP4862 W 19970908

OTHER SOURCE(S): MARPAT 128:230701
GI

L4 ANSWER 203 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



II

AB Title compds. RCOZCR1R2C(:X)ANR3R4 [(I); R = (substituted) alkyl; R1 = H, alkyl, PhCH2; R2 = (CO)m(CH2)nR5; m = 0, 1; n = 1, 2; R5 = Ph, heterocycle; X = O, (H,H); Z = CH2, NR6; R6 = H, alkyl, phenyl-alkyl; A = bond, proline; R3 = H, substituted alkyl, Ph, pyridinyl; R4 = H, substituted alkyl; NR3R4 = (substituted) heterocycle], useful as calcitonin gene-related peptide (CGRP) antagonists, were prepared Thus, 3,5-dibromo-N2-[4-(1,3-dihydro-2(2H)-oxo-benzimidazol-1-yl)-1-piperidinyl]carbonyl-D-tyrosine was reacted with 1-(4-pyridinyl)-piperazine, to give II (22%). In in-vitro binding studies with human CGRP-receptors, I had IC50 ≤10000 nM; in CGRP-antagonist in vitro tests, I was effective at doses from 10-11 to 10-5 M.

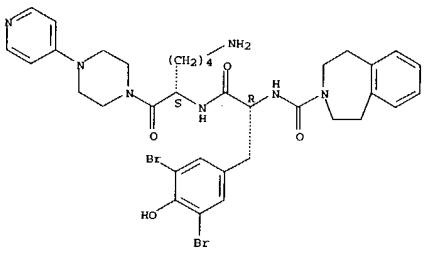
IT **204698-94-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of amino acids and their use as calcitonin gene-related peptide antagonists in pharmaceutical compns.)

RN 204698-94-2 CAPLUS

CN 3H-3-Benzazepine-3-carboxamide, N-[2-[[5-amino-1-[[4-(4-pyridinyl)-1-piperazinyl]carbonyl]pentyl]amino]-1-[(3,5-dibromo-4-hydroxyphenyl)methyl]-2-oxoethyl]-1,2,4,5-tetrahydro-, [R-(R*,S*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

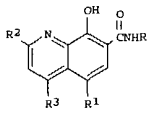
L4 ANSWER 203 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 204 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:180848 CAPLUS
DOCUMENT NUMBER: 128:243960
TITLE: 8-Hydroxy-7-substituted quinolines as anti-viral agents
INVENTOR(S): Vaillancourt, Valerie A.; Romines, Karen R.; Romero, Arthur G.; Tucker, John A.; Strohbach, Joseph W.; Bezencon, Olivier; Thaisrivongs, Suvit; et al.
PATENT ASSIGNEE(S): Pharmacia & Upjohn Co., USA
SOURCE: PCT Int. Appl., 280 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9811073	A1	19980319	WO 1997-US15310	19970905
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9741721	A1	19980402	AU 1997-41721	19970905
EP 927164	A1	19990707	EP 1997-939690	19970905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6310211	B1	20011030	US 1997-924683	19970905
JP 2002505660	T2	20020219	JP 1998-513685	19970905
US 6211376	B1	20010403	US 1999-425789	19991022
US 6252080	B1	20010626	US 1999-425564	19991022
US 6500842	B1	20021231	US 2001-14780	20011023

PRIORITY APPLN. INFO.: US 1996-25870P P 19960910
US 1997-50720P P 19970625
US 1997-924683 A3 19970905
WO 1997-US15310 W 19970905
OTHER SOURCE(S): MARPAT 128:243960
GI

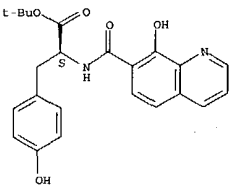


I

AB The present invention provides for 8-hydroxy-7-substituted quinoline compds. I (R = alkyl, alkylamino, alkoxyalkyl, etc.; R1 = H, F, Cl, Br,

L4 ANSWER 204 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Cf3, etc.; R2 = H, alkyl, OH, arylalkenyl, etc.; R3 = H, OH, CF3, C1-C3alkyl) are prepd. as anti-viral agents. Specifically, these compds. have anti-viral activity against the herpes virus, cytomegalovirus (CMV). Many of these compds. are also active against other herpes viruses, such as the varicella zoster virus, the Epstein-Barr virus, the herpes simplex virus and the human herpes virus type 8 (HHV-8).
IT **205038-81-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 8-hydroxy-7-substituted quinolines as anti-viral agents)
RN 205038-81-9 CAPLUS
CN L-Tyrosine, N-[(8-hydroxy-7-quinolinyl)carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

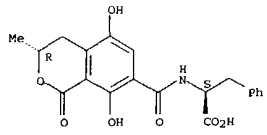
Absolute stereochemistry.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 205 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:172195 CAPLUS
DOCUMENT NUMBER: 128:240972
TITLE: Ochratoxin A acts as a photoactivatable DNA cleaving agent
AUTHOR(S): Gillman, Ivan G.; Yezek, Jennifer M.; Manderville, Richard A.
CORPORATE SOURCE: Department of Chemistry, Wake Forest University, Winston-Salem, NC, 27109-7486, USA
SOURCE: Chemical Communications (Cambridge) (1998), (6), 647-648
CODEN: CHCOFS; ISSN: 1359-7345
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ability of ochratoxin A to photoinduce DNA cleavage is described; in the presence of DNA the photoreaction yields the non-chlorinated derivative, ochratoxin B, while a hydroquinone derivative is produced under anaerobic conditions.
IT **205034-32-8P**
RL: BPN (Biosynthetic preparation); BIOL (Biological study); PREP (Preparation)
(ochratoxin A acts as a photoactivatable DNA cleaving agent)
RN 205034-32-8 CAPLUS
CN L-Phenylalanine, N-[[(3R)-3,4-dihydro-5,8-dihydroxy-3-methyl-1-oxo-1H-2-benzopyran-7-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 206 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:147347 CAPLUS
DOCUMENT NUMBER: 128:217634
TITLE: Preparation of protease-resistant B1-bradykinin receptor antagonists for treatment of inflammatory conditions
INVENTOR(S): Regoli, Domenico; Plante, Gerard E.; Gobeil, Fernand; Neugebauer, Witold A.; Zuccollo, Adriana; Catanzaro, Orlando L.
PATENT ASSIGNEE(S): Universite De Sherbrooke, Can.
SOURCE: PCT Int. Appl., 41 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

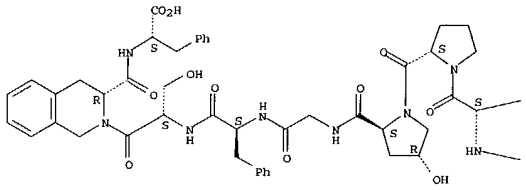
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9807746	A1	19980226	WO 1997-CA582	19970814
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9739358	A1	19980306	AU 1997-39358	19970814

PRIORITY APPLN. INFO.: US 1996-23971P P 19960819
WO 1997-CA582 W 19970814
OTHER SOURCE(S): MARPAT 128:217634
AB The present invention relates to novel B1-bradykinin (B1-BK) receptor antagonists A-Arg-Pro-B-Gly-Phe-Ser-C-D [I; A = H-D-Arg, Ac-Lys, H-D-Lys, H-Sar, Ac-Tyr-ε-Ahx-Lys, H-Sar-Tyr-ε-Ahx-Lys, H-Sar-Tyr(I2-3,5)-ε-Ahx-Lys; B = Pro, Hyp; C = Pro, D-1,2,3,5-tetrahydroisoquinoline-3-carbonyl (D-Tic), D-3-(2-naphthyl)alanyl (D-β-Nal); D = Leu-OH, Ile-OH; ε-Ahx = NH(CH2)5CO; with the proviso that C ≠ Pro when A does not contain ε-Ahx] which have a good affinity and selectivity therefor, some of which being at least partially resistant to enzymic degradation. The synthesis of the B1 receptors is induced during inflammation. Symptoms associated with inflammation (elevated hydrostatic pressure and plasma leakage or extravasation) have been observed in diabetic animal models [streptozotocin-induced diabetes (STZ)] as well as in spontaneously hypertensive rats (SHR). The present inventors confirm the presence of B1-BK receptors in these two models. B1-BK antagonists abolished the vasocontraction induced by B1-BK in SHR and STZ, and reduced the glycemia of diabetic animals to normal levels. The present B1-antagonists are useful for treating any condition wherein B1-receptor is expressed, particularly during inflammation, and more particularly wherein B1-receptor expression results in diabetic vasculopathy, other diabetic symptoms associated with an insulitis and a post-capillary resistance building as a consequence of the presence of a B1-receptor.
IT **185052-06-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of protease-resistant B1-bradykinin receptor antagonists for treatment of inflammatory conditions)

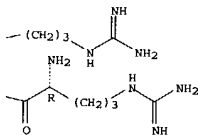
L4 ANSWER 206 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RN 185052-06-6 CAPLUS
CN L-Phenylalanine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-L-phenylalanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



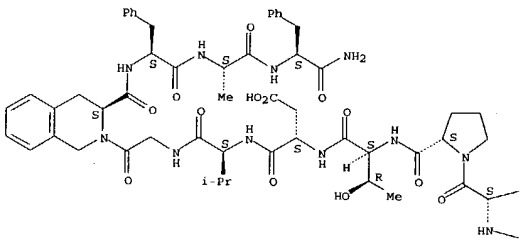
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 207 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1998:118 CAPLUS
DOCUMENT NUMBER: 128:110919
TITLE: From Micromolar to Nanomolar Affinity: A Systematic Approach To Identify the Binding Site of CGRP at the Human Calcitonin Gene-Related Peptide 1 Receptor
AUTHOR(S): Rist, Beate; Entzeroth, Michael; Beck-Sickinger, Annette G.
CORPORATE SOURCE: Department of Pharmacy, ETH Zuerich, Zurich, Switz.
SOURCE: Journal of Medicinal Chemistry (1998), 41(1), 117-123
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB CGRP Y0-28-37 is known as a selective CGRP1 receptor antagonist. To elucidate the essential requirements for its receptor interaction, the authors performed a variety of systematic approaches by modifying the C-terminal segments CGRP Y0-28-37 and CGRP 27-37. N-Terminal and C-terminal segments have been synthesized, as well as chimeras which combine segments of CGRP, adrenomedullin, and amylin. Furthermore, the authors carried out an Ala scan, a Phe scan, a D-amino acid scan and a Pro scan of CGRP 27-37. Addnl., single amino acids were replaced by those with similar biophys. properties. Receptor binding studies of all analogs were performed at human neuroblastoma cells SK-N-MC, which selectively express the hCGRP1 receptor. On the basis of the obtained results, the authors synthesized a series of ligands with multiple amino acid replacements to optimize the exchange at each position. This approach yielded to a series of high affinity ligands, including [D31,P34,F35] CGRP 27-37 which exhibits a 100-fold increased affinity compared to the unmodified segment. So far, this is the smallest CGRP analog that shows affinity in the nanomolar range.
IT **201613-69-6**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(from micromolar to nanomolar affinity: a systematic approach to identify the binding site of CGRP at the human calcitonin gene-related peptide 1 receptor)
RN 201613-69-6 CAPLUS
CN L-Phenylalaninamide, L-phenylalanyl-L-valyl-L-prolyl-L-threonyl-L-α-aspartyl-L-valylglycyl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-phenylalanyl-L-alanyl- (9CI) (CA INDEX NAME)

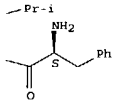
Absolute stereochemistry.

L4 ANSWER 207 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B

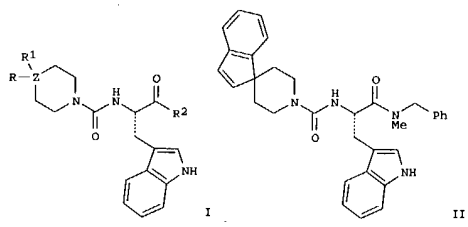


REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 208 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:798601 CAPLUS
DOCUMENT NUMBER: 128:13436
TITLE: Preparation of tryptophan urea derivatives as tachykinin receptor antagonists
INVENTOR(S): Maccoss, Malcolm; Oi, Hongbo; Shah, Shrenik K.
PATENT ASSIGNEE(S): Merck and Co., Inc., USA
SOURCE: Brit. UK Pat. Appl., 47 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
GB 2311523	A1	19971001	GB 1997-5861		19970321
PRIORITY APPLN. INFO.:			US 1996-14003P	P	19960325
			GB 1996-11786	A	19960606

OTHER SOURCE(S): MARPAT 128:13436
GI

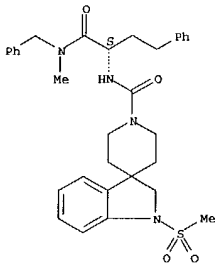


I II

AB Substituted title azacycles I [Z = N, R = CH2Ph, Ph, 2-MeOC6H4, 2-MeC6H4, R1 = absent; Z = C, R = Ph, R1 = NHOMe; R = CH2Ph, 2-oxo-1,2,3,4-tetrahydroquinazolin-1-yl, R1 = H; RZR1 = spiro-fused 1-indanyl, 3-indenyl, 1-methylsulfonyl-2,3-dihydroindol-3-yl, 1-acetyl-2,3-dihydroindol-3-yl; R2 = OCH2Ph wherein the Ph is substituted with 0-3 groups halo, Me, or CF3; or R2 = NR3-C1-4-alkylphenyl wherein the C1-4-alkyl may be linear or branched and the Ph may be substituted with 0-3 groups halo, Me, OMe, CF3; R3 = H, Me, Et] and pharmaceutically acceptable salts thereof are tachykinin receptor antagonists useful in the treatment of inflammatory diseases, pain or migraine, and asthma. In particular, compds. I are neurokinin antagonists. Thus, amidation of 1.967 g Boc-Trp-OH (Boc = Me3CO2C) with 0.87 mL MeNHCH2Ph gave 2.56 g of the corresponding amide, which underwent deprotection with CF3CO2H, condensation with carbonyldiimidazole, and urea formation with spiro[1H-indene-1,4'-piperidine] hydrochloride to give title compound II (L-743,516). I and related Trp derivs. showed IC50 values of >1000 to 1 nM for human neurokinin 1 (NK1) antagonist activity.
IT **199110-44-6P**

L4 ANSWER 208 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of tryptophan urea derivs. as tachykinin receptor antagonists)
RN 199110-44-6 CAPLUS
CN Spiro[3H-indole-3,4'-piperidine]-1'-carboxamide, 1,2-dihydro-N-[(1S)-1-[[methyl(phenylmethyl)amino]carbonyl]-3-phenylpropyl]-1-(methylsulfonyl)-(9CI) (CA INDEX NAME)

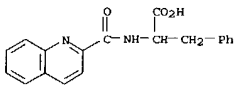
Absolute stereochemistry.



L4 ANSWER 209 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:794681 CAPLUS
DOCUMENT NUMBER: 128:75653
TITLE: Tandem UPS: sequential mono- and dialkylation of resin-bound glycine via automated synthesis
AUTHOR(S): Griffith, David L.; O'Donnell, Martin J.; Pottorf, Richard S.; Scott, William L.; Porco, John A., Jr.
CORPORATE SOURCE: Argonaut Technologies, San Carlos, CA, 94070, USA
SOURCE: Tetrahedron Letters (1997), 38(51), 8821-8824
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A method has been developed for the synthesis of racemic α,α-disubstituted amino acids by a tandem alkylation process ("Tandem UPS") on solid-support. Consecutive alkylations of Wang resin-bound benzophenone imines of glycine afforded unnatural, disubstituted amino acid derivs. Automated chemical synthesis was used to efficiently optimize conditions for both formation and hydrolysis of resin-bound disubstituted benzophenone imines and to generate a matrix of disubstituted amino acid derivs.
IT **200573-87-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(sequential mono- and dialkylation of resin-bound glycine via automated synthesis)
RN 200573-87-1 CAPLUS
CN Phenylalanine, N-(2-quinolinylcarbonyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)

CM 1

CRN 197392-59-9
CMF C19 H16 N2 O3

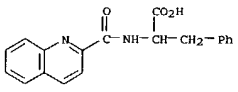


CM 2

CRN 76-05-1
CMF C2 H F3 O2

L4 ANSWER 209 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 210 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:707354 CAPLUS
DOCUMENT NUMBER: 127:307645
TITLE: Solid-phase synthesis of unnatural amino acids using unactivated alkyl halides
AUTHOR(S): O'donnell, Martin J.; Lugar, Charles W.; Pottorf, Richard S.; Zhou, Changyou; Scott, William L.; Cwi, Cynthia L.
CORPORATE SOURCE: Department of Chemistry, Indiana University-Purdue University at Indianapolis, Indianapolis, IN, 46202, USA
SOURCE: Tetrahedron Letters (1997), 38(41), 7163-7166
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Conditions were developed for the efficient alkylation of the resin-bound benzophenone imine of glycine with a variety of unreactive alkyl halides. Alkylations were accomplished at room temperature in NMP using the phosphazene-type base BEMP.
IT **197392-59-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid-phase synthesis of unnatural amino acids using unactivated alkyl halides)
RN 197392-59-9 CAPLUS
CN Phenylalanine, N-(2-quinolinylcarbonyl)- (9CI) (CA INDEX NAME)

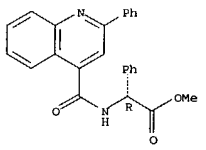


L4 ANSWER 211 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:674193 CAPLUS
DOCUMENT NUMBER: 127:355226
TITLE: In vitro and in vivo characterization of NK3 receptors in the rabbit eye by use of selective non-peptide NK3 receptor antagonists
AUTHOR(S): Medhurst, Andrew D.; Hay, Douglas W. P.; Parsons, Andrew A.; Martin, Lenox D.; Griswold, Don E.
CORPORATE SOURCE: Department of Neurosciences Research, SmithKline Beecham Pharmaceuticals, Essex, CM19 5AW, UK
SOURCE: British Journal of Pharmacology (1997), 122(3), 469-476
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 1 Inhibition of NK3 receptor agonist-induced contraction in the rabbit isolated iris sphincter muscle was used to assess the in vitro functional activity of three 2-phenyl-4-quinolinecarboxamides, members of a novel class of potent and selective non-peptide NK3 receptor antagonists. In addition, an in vivo correlate of this in vitro response, namely NK3 receptor agonist-induced miosis in conscious rabbits, was characterized with some of these antagonists. 2 In vitro senktide (succinyl-[Asp9, MePhe8]-substance P (6-11) and [MePhe7]-neurokinin B[MePhe7]-NKB) were potent contractile agents in the rabbit iris sphincter muscle but exhibited quite different profiles. Senktide produced monophasic log concentration-effect curves with a mean pD2=9.03±0.06 and mean nH=1.2±0.02 (n= 14). In contrast, [MePhe7]-NKB produced shallow log concentration-effect curves which often appeared biphasic (nH=0.54±0.04, n=8), preventing the accurate determination of pD2 values. 3 The contractile responses to the NK3 receptor agonist senktide were antagonized in a surmountable and concentration-dependent manner by SB 223412 [(-)-(S)-N-(α-ethylbenzyl)-3-hydroxy-2-phenylquinoline-4-carboxamide; 3-30 nM, pA2 = 8.4, slope= 1.8±0.3, n=4], SB 222200 [(-)-(S)-N-(α-ethylbenzyl)-3-methyl-2-phenylquinoline-4-carboxamide; 30-300 nM, pA2= 7.9, slope= 1.4±0.06, n=4] and SB 218795 [(-)-(R)-N-(α-methoxycarbonylbenzyl)-2-phenylquinoline-4-carboxamide; 0.3 and 3 μM apparent pKB= 7.4±0.06, n=6]. 4 Contractile responses to the NK3 receptor agonist [MePhe7]-NKB in the rabbit iris sphincter muscle were unaffected by SB 218795 (0.3 and 3 μM, n=8). In contrast, SB 223412 (30 and 300 μM, n=4) and SB 222200 (0.3 and 3 μM, n=4) inhibited responses to low concns. (≤ 1 nM), to a greater extent than higher concns. (>1 nM) of [MePhe7]-NKB. Furthermore, log concentration-effect curves to [MePhe7]-NKB became steeper and monophasic in the presence of each antagonist. 5 SB 218795 (3 μM, n=4) had no effect on contractions induced by transmural nerve stimulation (2 Hz) or substance P, exemplifying the selectivity of this class of antagonist for functional NK3 receptors over NK1 receptors in the rabbit. 6 In vivo, senktide (1, 10 and 25 μg i.v.,i.e. 1.2, 11.9 and 29.7 nmol, resp.) induced concentration-dependent bilateral miosis in conscious rabbits (maximum pupillary constriction =4.25±0.25 mm; basal pupillary diameter 7.75±0.48 mm; n=4). The onset of miosis was within 2-5 min of application of senktide and responses lasted up to 30 min. Responses to two i.v. administrations of 25 μg senktide given 30 min apart revealed no evidence of tachyphylaxis. Topical administration of atropine (1%) to the eye enhanced pupillary responses to 25 μg senktide. This was probably due to the mydriatic effect of atropine since it significantly increased baseline pupillary diam. from 7.0±0.4 mm to 9.0±0.7 mm (n=4), thereby increasing the max. capacity for miosis. Senktide-induced miosis was inhibited by SB 222200 (1 and 2 mg kg-1, i.v., i.e. 2.63 and 5.26 μmol kg-1; max. inhibition 100%; n=3-4), SB 223412 (0.5 and 1 mg kg-1, i.v., i.e. 1.31 and 2.61 μmol kg-1; max. inhibition 100%; n=3), SB 218795 (0.5 and 1 mg kg-1, i.v., i.e. 1.26 and 2.52 μmol kg-1; max. inhibition 78%; n=3), and the structurally distinct NK3 receptor antagonist SR 142801 [(S)-(N)-(1-(3-(1-benzoyl-3-(3,4-dichlorophenyl)piperidin-3-yl)propyl)-4-phenylpipiperidin-4-yl)-N-methylacetamide; 1.5 mg kg-1, i.v.,i.e. 2.47 μmol kg-1, max. inhibition 92%; n=3]. Opical administration of senktide (25 μg; 29.7 nmol) to the eye induced unilateral miosis in the treated eye only. At this dose there was no significant difference (P<0.05) between pupillary constriction obtained by topical or i.v. senktide, and topically administered atropine had no significant effect on responses to topical senktide (n=4). 8 [MePhe7]-NKB (125, 250 and 500 μg, i.v., i.e. 98.31, 196.62 and 393.24 nmol, resp.) also induced bilateral miosis in conscious rabbits (max. pupillary constriction=4.13±0.30 mm; n=4), but in contrast to in vitro studies this agonist was approx. 100 fold less potent than senktide. [MePhe7]-NKB-induced miosis was inhibited by SB 222200 (5 mg kg-1, i.v., i.e. 13.14 μmol kg-1; max. inhibition 69%; n=3). 9 In summary, SB 223412, SB 222200 and SB 218795 are potent and selective antagonists of NK3 receptor-mediated contraction in the rabbit isolated iris sphincter muscle. In addn., NK3 receptor agonist-induced miosis in conscious rabbits is a good in vivo correlate of the in vitro rabbit iris sphincter muscle prepn. and appears to be a useful model for characterizing the pharmacodynamic profile and efficacy of structurally distinct NK3 receptor antagonists, such as SB 222200, SB 223412, SB 218795 and SR 142801.

IT **174635-53-1**, SB 218795
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(characterization of NK3 receptors in the rabbit eye by use of selective non-peptide NK3 receptor antagonists)
RN 174635-53-1 CAPLUS
CN Benzeneacetic acid, α-[[(2-phenyl-4-quinolinyl)carbonyl]amino]-, methyl ester, (αR)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



L4 ANSWER 212 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:594721 CAPLUS
DOCUMENT NUMBER: 127:278064
TITLE: Substituted 4-hydroxyphenylalkanoic acid derivatives with agonist activity to PPAR-gamma
INVENTOR(S): Willson, Timothy Mark; Mook, Robert Anthony, Jr.; Kaldor, Istvan; Henke, Brad Richard; Deaton, David Norman; Collins, Jon Loren; Cobb, Jeffrey Edmond; et al.
PATENT ASSIGNEE(S): Glaxo Group Ltd., UK
SOURCE: PCT Int. Appl., 157 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9731907	A1	19970904	WO 1997-EP916	19970226
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2247443	AA	19970904	CA 1997-2247443	19970226
AU 9720935	A1	19970916	AU 1997-20935	19970226
AU 717699	B2	20000330		
ZA 9701645	A	19971210	ZA 1997-1645	19970226
EP 888317	A1	19990107	EP 1997-906130	19970226
EP 888317	B1	20010912		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
CN 1218460	A	19990602	CN 1997-193988	19970226
CN 1093124	B	20021023		
BR 9707786	A	19990727	BR 1997-7786	19970226
JP 2000507216	T2	20000613	JP 1997-530586	19970226
JP 3255930	B2	20020212		
NZ 331381	A	20000623	NZ 1997-331381	19970226
IL 125796	A1	20010614	IL 1997-125796	19970226
AT 205485	E	20010915	AT 1997-906130	19970226
ES 2163125	T3	20020116	ES 1997-906130	19970226
PT 888317	T	20020328	PT 1997-97906130	19970226
SK 282753	B6	20021203	SK 1998-1163	19970226
HR 970110	B1	20030630	HR 1997-970110	19970226
TW 391958	B	20000601	TW 1997-86102826	19970307
US 6294580	B1	20010925	US 1998-125750	19980825
NO 9803940	A	19981027	NO 1998-3940	19980827
HK 1015369	A1	20020215	HK 1999-100498	19990205

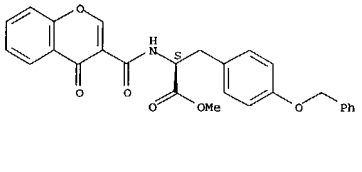
PRIORITY APPLN. INFO.: GB 1996-4242 A 19960228
WO 1997-EP916 W 19970226

OTHER SOURCE(S): MARPAT 127:278064

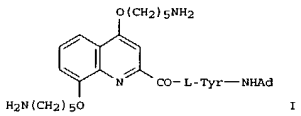
AB Compds. 4-(A-B-O)C6H4-Q-CHZCO2R1 [A = (un)substituted Ph, heterocyclyl, fused bicyclic ring; B = alkylene, heterocyclyl; Q = alkylene; R1 = H, alkyl; Z = alkylenephenyl, NR3R4 (R3 = H, alkyl; R4 = YXOTR5, YCH(OH)TR5 with Y = bond, alkylene, alkenylene, cycloalkylene, etc. and T = bond, O, etc. and R5 = alkyl, cycloalkyl, (un)substituted Ph)] were prepared and their agonist activity to PPAR-gamma determined E.g., O-benzyl L-tyrosine, dicyclohexylamine, and 1-benzoylacetone were refluxed in MeOH to give 3-(4-benzyloxyphenyl)-2(S)-(1-methyl-3-oxo-3-phenylpropenylamino)propionic acid dicyclohexylamine salt.

IT **196808-22-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of (hydroxyphenyl)alkanoic acids with agonist activity to PPAR-gamma)
RN 196808-22-7 CAPLUS
CN L-Tyrosine, N-[(4-oxo-4H-1-benzopyran-3-yl)carbonyl]-O-(phenylmethyl)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 213 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:520078 CAPLUS
DOCUMENT NUMBER: 127:205826
TITLE: Design, synthesis and pharmacological test of a quinoline based, nonpeptidic analog of neurotensin(8-13)
AUTHOR(S): Hong, Feng; Pang, Yuan-Ping; Cusack, Bernadette; Richelson, Elliott
CORPORATE SOURCE: Neurochemistry Research, Mayo Foundation for Medical Education and Research, Jacksonville, FL, 32224, USA
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1997), (14), 2083-2088
CODEN: JCPRB4; ISSN: 0300-922X
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



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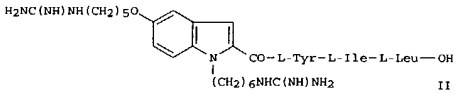

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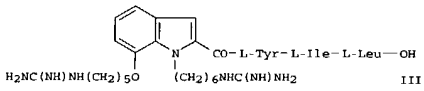
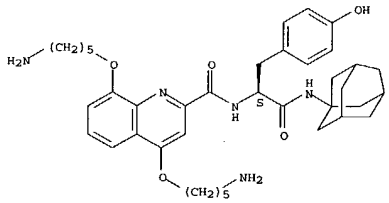


III

AB Based on the multiple template approach to developing nonpeptidic mimetics of neuropeptides, the design, synthesis and pharmacol. testing of a quinoline based analog of neurotensin(8-13) I (Ad = 1-adamantyl) are reported. The newly synthesized quinoline analog is found to be less active in binding to the neurotensin receptors than previously reported mimetics II and III, which are partial nonpeptidic analogs of neurotensin(8-13). The correct structures of II and III are reported,

L4 ANSWER 213 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
here, since this study led to the discovery of a mistake in the previously reported literature procedure for alkylation at position-3 of Et indole-2-carboxylate.
IT **194673-23-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and pharmacol. testing of a quinoline based, nonpeptidic analog of neurotensin(8-13))
RN 194673-23-9 CAPLUS
CN 2-Quinolinecarboxamide, 4,8-bis[(5-aminopentyl)oxy]-N-[1-[(4-hydroxyphenyl)methyl]-2-oxo-2-(tricyclo[3.3.1.13,7]dec-1-ylamino)ethyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 214 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:475133 CAPLUS
DOCUMENT NUMBER: 127:162123
TITLE: Peptides having bradykinin antagonist action
INVENTOR(S): Henke, Stephan; Anagnostopulos, Hiristo; Breipohl, Gerhard; Knolle, Jochen; Stechl, Jens; Scholkens, Bernward; et al.
PATENT ASSIGNEE(S): Hoechst A.-G., Germany
SOURCE: U.S., 26 pp., Cont. of U.S. Ser. No. 236,018.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5648333	A	19970715	US 1995-487442	19950607
DD 284030	A5	19901031	DD 1989-331416	19890802
ZA 8906068	A	19910130	ZA 1989-6068	19890809
DE 3926822	A1	19910221	DE 1989-3926822	19890814
DE 4013270	A1	19911031	DE 1990-4013270	19900426
RU 2083586	C1	19970710	RU 1992-5052703	19921012
LT 3375	B	19950825	LT 1993-717	19930625

PRIORITY APPLN. INFO.:
DE 1988-3839581 A 19881124
DE 1989-3916291 A 19890519
DE 1989-3926225 A 19890603
US 1989-374162 B2 19890630
DE 1989-3926822 A 19890814
DE 1990-4013270 A 19900426
US 1990-565270 B2 19900810
US 1991-690297 B1 19910424
US 1991-746149 B1 19910814
US 1992-837090 B2 19920218
US 1992-841766 B1 19920302
US 1992-969523 B2 19921030
US 1992-982052 B2 19921125
US 1993-12849 B1 19930203
US 1994-236018 A1 19940502

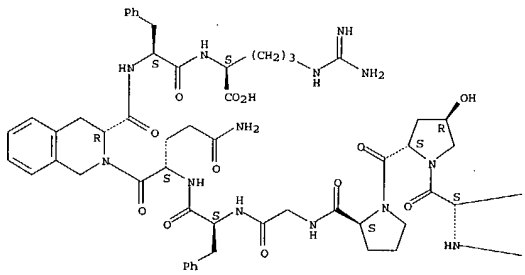
OTHER SOURCE(S): MARPAT 127:162123

AB Peptides A-B-C-E-F-K-P-G-M-F [A = H, alkyl, alkanoyl, cycloalkyl, aryl, etc.; B = basic amino acid which may be substituted in side chain; C = G'-G'-Gly or G'-NH(CH2)nCO, where G' = heterocyclylcarbonyl and n = 2-8; E = aromatic amino acid radical; F, M = bond or amino acid which may be substituted in side chain; K = bond or NH(CH2)xCO, where x = 1-4; P = D-Tic (Tic = 1,2,3,4-tetrahydroisoquinolin-3-ylcarbonyl); G = bond or G'] were prepared as bradykinin antagonists. Thus, H-D-Arg-Arg-Hyp-Pro-Gly-Phe-Ser-D-Tic-Phe-Arg-OH was prepared by the solid phase method and assayed for bradykinin antagonist activity (IC50 = 4.6 x 10-6 M).
IT **193618-41-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(peptides having bradykinin antagonist action)
RN 193618-41-6 CAPLUS
CN L-Arginine, D-arginyl-L-arginyl-(4R)-4-hydroxy-L-prolyl-L-prolylglycyl-L-phenylalanyl-L-glutaminyl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 214 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



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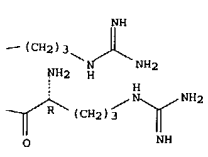

L4 ANSWER 215 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:465088 CAPLUS
DOCUMENT NUMBER: 127:95204
TITLE: Preparation of quinoline-4-carboxamides and their use as neurokinin-3 and neurokinin-2 receptor antagonists
INVENTOR(S): Giardina, Giuseppe Arnaldo Maria; Grugni, Mario; Raveglia, Luca Francesco; Farina, Carlo
PATENT ASSIGNEE(S): Smithkline Beecham S.P.A., Italy; Giardina, Giuseppe Arnaldo Maria; Grugni, Mario; Raveglia, Luca Francesco; Farina, Carlo
SOURCE: PCT Int. Appl., 79 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9719926	A1	19970605	WO 1996-EP5207	19961122
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
IT 1307330	B1	20011030	IT 1996-MI1688	19960802
CA 2238328	AA	19970605	CA 1996-2238328	19961122
AU 9710318	A1	19970619	AU 1997-10318	19961122
ZA 9609811	A	19980522	ZA 1996-9811	19961122
CN 1207729	A	19990210	CN 1996-199747	19961122
BR 9611757	A	19990406	BR 1996-11757	19961122
EP 1019377	A1	20000719	EP 1996-941025	19961122
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO				
JP 2000513325	T2	20001010	JP 1997-520158	19961122
TW 409123	B	20001021	TW 1996-85114501	19961123
NO 9802333	A	19980722	NO 1998-2333	19980522
US 2002068827	A1	20020606	US 2001-994402	20011126

PRIORITY APPLN. INFO.:
IT 1995-MI2462 A 19951124
IT 1996-MI1688 A 19960802
WO 1996-EP5207 W 19961122
US 1998-77262 B1 19980806
US 2000-515336 B1 20000605

OTHER SOURCE(S): MARPAT 127:95204
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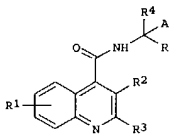
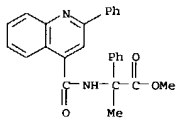


I

AB The title compds. [I; A = (un)substituted aryl, C5-7 cycloalkdienyl, (un)substituted single or fused ring aromatic heterocyclyl; R = (un)substituted C1-6 alkyl, C3-7 cycloalkyl, C3-7 cycloalkylalkyl, (un)substituted Ph, an optionally substituted five-membered heteroarom. ring, etc.; R1 = hydrogen or up to four substituents selected from C1-6 alkyl, C1-6 alkenyl, aryl, C1-6 alkoxy, hydroxy, halogen, nitro, cyano, carboxy, carboxamido, sulfonamido, C1-6 alkoxycarbonyl, trifluoromethyl, alkoxy, phthalimido, (un)substituted amino, etc.; R2 = hydrogen, C1-6 alkyl, hydroxy, halogen, cyano, (un)substituted amino, etc.; R3 = C1-6 alkyl, C3-7 cycloalkyl, C4-7 cycloalkylalkyl, (un)substituted aryl, (un)substituted single or fused ring aromatic heterocyclyl; R4 = hydrogen, C1-6 alkyl], useful as neurokinin 3 and neurokinin 2 receptor antagonists, are prepared Thus, (S)-N-(α-ethylbenzyl)-3-(2-aminoethoxy)-2-phenylquinoline-4-carboxamide was reacted with α,α'-dibromo-o-xylene and salified with HCl, producing (S)-N-(α-ethylbenzyl)-3-[2-(2-isoindolinyl)ethoxy]-2-phenylquinoline-4-carboxamide dihydrochloride (m.p. 95°; decomposition) which demonstrated a binding affinity in human neurokinin-3 receptors (expressed in CHO cell lines) against [125I]-[Me-Phe7]-neurokinin B of 1.2 nM.

IT **191796-50-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinoline-4-carboxamides and their use as neurokinin-3 and neurokinin-2 receptor antagonists)

RN 191796-50-6 CAPLUS
CN Benzeneacetic acid, α-methyl-α-[[(2-phenyl-4-quinolinyl)carbonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)

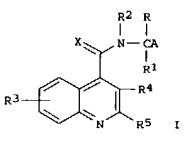


L4 ANSWER 216 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:461591 CAPLUS
DOCUMENT NUMBER: 127:95205
TITLE: Preparation of quinoline-derivative NK3 receptor antagonists
INVENTOR(S): Giardina, Giuseppe Arnaldo Maria; Farina, Carlo; Grugni, Mario; Raveglia, Luca Francesco
PATENT ASSIGNEE(S): Smithkline Beecham S.P.A., Italy; Giardina, Giuseppe Arnaldo Maria; Farina, Carlo; Grugni, Mario; Raveglia, Luca Francesco
SOURCE: PCT Int. Appl., 101 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9719927	A1	19970605	WO 1996-EP5209	19961122
W: JP, US				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 874827	A1	19981104	EP 1996-939926	19961122
EP 874827	B1	20030521		
R: BE, CH, DE, ES, FR, GB, IT, LI, NL				
JP 2000512614	T2	20000926	JP 1997-520159	19961122
US 2003195204	A1	20031016	US 2002-140452	20020507

PRIORITY APPLN. INFO.:
GB 1995-24104 A 19951124
WO 1996-EP5209 W 19961122
US 1998-77156 B1 19980521

OTHER SOURCE(S): MARPAT 127:95205
GI

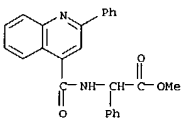


I

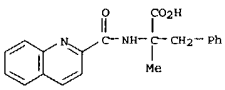
AB The title compds. [I; A = (un)substituted Ph, (un)substituted naphthyl, C5-7 cycloalkdienyl, (un)substituted heterocyclyl; R = C1-8 alkyl, C3-7 cycloalkyl, C4-7 cycloalkylalkyl, (un)substituted Ph, phenylalkyl, etc.; R1, R2 = H, C1-6 alkyl, or together form a (CH2)n, etc.; n = 3-5; R3, R4 = H, C1-6 alkyl, C1-6 alkenyl, aryl, C1-6 alkoxy, hydroxy, halogen, nitro, cyano, carboxy, carboxamido, sulfonamido, C1-6 alkoxycarbony, trifluoromethyl, acyloxy, phthalimido, (un)substituted amino, etc.; R5 = C1-6 alkyl, C3-7 cycloalkyl, etc.; X = O, S, NC.tplbond.N; etc.], which are NK3 receptor antagonists (no data), are prepared Thus, α-methylbenzylamine was amidated with 2-phenylquinoline-4-carbonyl chloride, producing N-(α-methylbenzyl)-2-phenyl-4-quinolinecarboxamide, m.p. 156-157°.

IT **174635-51-9P**
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

RN 174635-51-9 CAPLUS
CN Benzeneacetic acid, α-[[(2-phenyl-4-quinolinyl)carbonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)



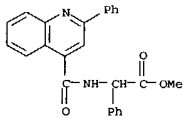
L4 ANSWER 217 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:348323 CAPLUS
DOCUMENT NUMBER: 127:81757
TITLE: The solid phase synthesis of α,α-disubstituted unnatural amino acids and peptides (di-UPS)
AUTHOR(S): Scott, William L.; Zhou, Changyou; Fang, Zhiqiang; O'Donnell, Martin J.
CORPORATE SOURCE: Res. Technologies Proteins, Lilly Res. Labs., Indianapolis, IN, 46285, USA
SOURCE: Tetrahedron Letters (1997), 38(21), 3695-3698
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 127:81757
AB This paper reports a new, mild procedure (di-UPS) for the solid phase synthesis of racemic α,α-disubstituted amino acids and epimeric α,α-disubstituted terminal amino acid residues in a resin-bound peptide. The synthetic route is compatible with most protected amino acid side chains and can be used in a continuing solid phase synthesis. Di-UPS should find a wide applicability in the design and solid phase synthesis of hybrid amino acids and peptides and the construction of basis units for combinational chemical
IT **191675-94-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid phase synthesis of disubstituted unnatural amino acids and peptides)
RN 191675-94-2 CAPLUS
CN Phenylalanine, α-methyl-N-(2-quinolinylcarbonyl)- (9CI) (CA INDEX NAME)



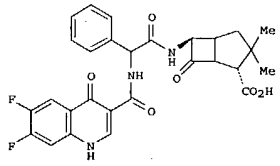
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 218 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:320920 CAPLUS
DOCUMENT NUMBER: 126:338400
TITLE: Discovery of a Novel Class of Selective Non-Peptide Antagonists for the Human Neurokinin-3 Receptor. 1. Identification of the 4-Quinolinecarboxamide Framework
AUTHOR(S): Giardina, Giuseppe A. M.; Sarau, Henry M.; Farina, Carlo; Medhurst, Andrew D.; Grugni, Mario; Raveglia, Luca F.; Schmidt, Dulcie B.; Rigolio, Roberto; Luttmann, Mark; Vecchietti, Vittorio; Hay, Douglas W. P.
CORPORATE SOURCE: Department of Chemistry, SmithKline Beecham S.p.A., Baranzate, 20021, Italy
SOURCE: Journal of Medicinal Chemistry (1997), 40(12), 1794-1807
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A novel class of potent and selective non-peptide neurokinin-3 (NK-3) receptor antagonists, featuring the 4-quinolinecarboxamide framework, was designed based upon chemical diverse NK-1 receptor antagonists. The novel compds., prompted by chemical modifications of the prototype, were characterized by binding anal. using a membrane preparation of chinese hamster ovary (CHO) cells expressing the human neurokinin-3 receptors (hNK-3-CHO), and clear structure-activity relationships (SARs) were established. From SARs, (R)-N-[α-(methoxycarbonyl)benzyl]-2-phenylquinoline-4-carboxamide (I, SB 218795, hNK-3-CHO binding Ki = 13 nM) emerged as one of the most potent compds. of this novel class. Selectivity studies vs. the other neurokinin receptors (hNK-2-CHO and hNK-1-CHO) revealed that 65 is about 90-fold selective for hNK-3 vs. hNK-2 receptors (hNK-2-CHO binding Ki = 1221 nM) and over 7000-fold selective vs. hNK-1 receptors (hNK-1-CHO binding Ki = >100 μM). In vitro functional studies in rabbit isolated iris sphincter muscle preparation demonstrated that I a competitive antagonist of the contractile response induced by the potent and selective NK-3 receptor agonist senktide with a Kb = 43 nM. Overall, the data indicate that I is a potent and selective hNK-3 receptor antagonist and a useful lead for further chemical optimization.
IT **174635-51-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of quinolinecarboxamide-containing nonpeptide neurokinin-3 receptor antagonists)
RN 174635-51-9 CAPLUS
CN Benzeneacetic acid, α-[[(2-phenyl-4-quinolinyl)carbonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 218 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



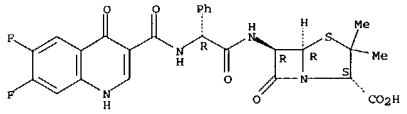
L4 ANSWER 219 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:316770 CAPLUS
DOCUMENT NUMBER: 127:47593
TITLE: Susceptibility of Pseudomonas aeruginosa of various pyocin types to the newly synthesized ampicillin derivative, N-(6,7-difluoroquinolonyl)ampicillin
AUTHOR(S): Chen, C. H.; Tsou, T. L.; Chiang, H. Y.; Lee, S. H.; Lee, F.; Lee, J. H.; Wang, T. M.; Liu, Y. T.
CORPORATE SOURCE: Section of Bacteriology, Division of Clinical Pathology, National Defence Medical Center, Tri-Service General Hospital, Taipei, Taiwan
SOURCE: Journal of Antimicrobial Chemotherapy (1997), 39(3), 325-330
CODEN: JACHDX; ISSN: 0305-7453
PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I

AB Six hundred and thirty-two isolates of Pseudomonas aeruginosa of 17 pyocin types were collected in 1993 in Taiwan. Types 1, 10, 3, 35 and 12 were the most common pyocin types identified in Taiwan with isolation frequencies of 47.3%, 24.4%, 7.6%, 3.6% and 2.2%, resp. Several pyocin subtypes were determined All pyocin types (one isolate of each tested) were resistant to ampicillin and nalidixic acid, but sensitive to fluoroquinolone antibiotics, such as norfloxacin and enoxacin, indicating that cross-resistance to quinolone antibiotics of nalidixic acid and fluoroquinolone derivs. has not developed. A new ampicillin derivative of 6,7-difluoroquinolonic acid, N-(6,7-difluoroquinolonyl)-ampicillin (AU-1, I), was synthesized by coupling ampicillin with 6,7-difluoroquinolonic acid (FP-3). I was much more active than either ampicillin or FP-3 alone against all pyocin types of P. aeruginosa and induced filamentation in most growing cells.
IT **190902-80-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(susceptibility of Pseudomonas aeruginosa of various pyocin types to (difluoroquinolonyl)ampicillin)
RN 190902-80-8 CAPLUS
CN 4-Thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid, 6-[[(2R)-[[(6,7-difluoro-1,4-dihydro-4-oxo-3-quinolinyl]carbonyl]amino]phenylacetyl]amino]-3,3-dimethyl-7-oxo-, (2S,5R,6R)- (9CI) (CA INDEX NAME)

L4 ANSWER 219 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
Absolute stereochemistry.



L4 ANSWER 220 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

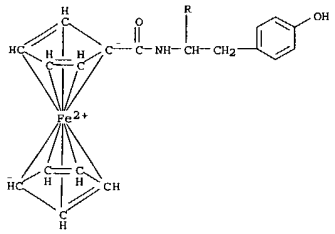
ACCESSION NUMBER: 1997:290042 CAPLUS
DOCUMENT NUMBER: 126:293586
TITLE: Ferrocenoyl Amino Acids: A Synthetic and Structural Study
AUTHOR(S): Kraatz, Heinz-Bernhard; Lusztyk, Janusz; Enright, Gary D.
CORPORATE SOURCE: Supramolecular Chemistry and Biology Group Steacie Institute of Molecular Science, National Research Council of Canada, Ottawa, ON, K1A 0R6, Can.
SOURCE: Inorganic Chemistry (1997), 36(11), 2400-2405
CODEN: INOCAJ; ISSN: 0020-1669
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 126:293586

AB Ester-protected amino acids were coupled to ferrocenecarboxylic acid using the DCC/HOBt protocol to give ferrocenoyl N-amino acids (amino acid = Glu(OBz)2 (2a), Gly(OEt) (2b), Pro(OBz) (2c), Cys(SBz)OMe (2d), Ala(OBz) (2e), Tyr(OBz) (2f), Phe(OBz) (2g)). All products were fully characterized. The intermediate hydroxybenzotriazole active ester FcCOOBt (3) was isolated and fully characterized. The solid state structures of 2a, 2d, and 3 were determined by single-crystal x-ray diffraction. 2A: monoclinic space group P21 with a 11.8142(5), b 9.7560(5), c 22.9456(10) Å, β 90.246(5)°, Z = 2, R = 0.046. 2D: orthorhombic space group P212121 with a 9.957(2), b 11.680(2), c 36.452(2) Å, Z = 4, R = 0.065. The solid state structures of 2a and 2d show extensive C:O···H-N H bonding. 3: Triclinic space group P.hivin.1 with a 7.0391(5), b 10.7922(7), c 11.1690(7) Å, α 108.071(5), β 107.957(5), γ 103.896(5)°, Z = 2, R = 0.030. The long ester bond distance of 1.427(2) Å provides a rationale for its inherent reactivity toward primary and secondary amines. Some of the ester-protected ferrocenoyl amino acids were also studied by cyclic voltammetry.

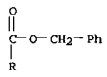
IT **189116-56-1P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)
RN 189116-56-1 CAPLUS
CN Ferrocene, [[[1-[(4-hydroxyphenyl)methyl]-2-oxo-2-(phenylmethoxy)ethyl]amino]carbonyl]-, (S)- (9CI) (CA INDEX NAME)

L4 ANSWER 220 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 2-A



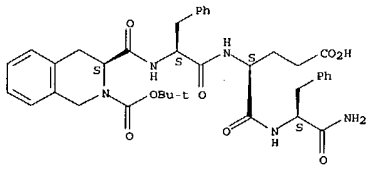
L4 ANSWER 221 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:287115 CAPLUS
DOCUMENT NUMBER: 127:30759
TITLE: Potency comparison of peptidomimetic inhibitors against HIV-1 and HIV-2 proteinases: design of equipotent lead compounds
AUTHOR(S): Weber, Jan; Majer, Pavel; Litera, Jaroslav; Urban, Jan; Soucek, Milan; Vondrasek, Jiri; Konvalinka, Jan; Novek, Petr; Sedlacek, Juraj; Strop, Petr; Krausslich, Hans-Georg; Pichova, Iva
CORPORATE SOURCE: Dep. Biochem., Inst. Org. Chem. Biochem., Acad. Sci. Czech Republic, Prague, 166 10, Czech Rep.
SOURCE: Archives of Biochemistry and Biophysics (1997), 341(1), 62-69
CODEN: ABBIA4; ISSN: 0003-9861
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English

AB HIV-1 and HIV-2 proteinases (PR) are responsible for the processing of viral polyproteins, a step that is crucial for the formation of infectious virus particles. PR represents one of the most important targets for antiviral chemotherapy. Inhibitors of HIV-1 PR usually exhibit a 10- to 100-fold weaker affinity for HIV-2 PR. To design subnanomolar inhibitors for both HIV-1 and HIV-2 PRs, we prepared a series of compds. varying in the type of scissile bond replacement as well as in the P1, P1', and P2' side chains. While inhibitors containing reduced amide, hydroxyethylamine and statine isosteres had Ki values in the range of 10-10-10-9 M against HIV-1 PR, their activities against HIV-2 PR were several orders of magnitude lower. Glutamic acid was identified to be the optimal P2' residue for both PRs. HIV-2 PR was shown to be more sensitive to P2' Glu→Gln replacement. Using this data set we were able to design and prepare hydroxyethylene isostere containing inhibitors that were equipotent against both PRs.

IT **190667-94-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(potency comparison of peptidomimetic inhibitors against HIV-1 and HIV-2 proteinases)
RN 190667-94-8 CAPLUS
CN L-Phenylalaninamide, (3S)-2-[(1,1-dimethylethoxy)carbonyl]-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-phenylalanyl-L-α-glutamyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



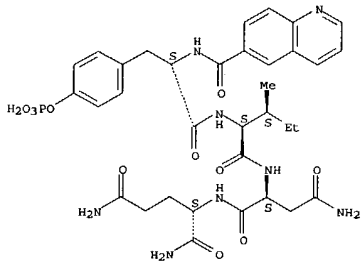
L4 ANSWER 222 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:283758 CAPLUS
DOCUMENT NUMBER: 126:264364
TITLE: Acylated oligopeptide derivatives having cell signal inhibiting activity
INVENTOR(S): Garcia-Echeverria, Carlos; Gay, Brigitte; Furet, Pascal; Rahuel, Joseph; Caravatti, Giorgio; Fretz, Heinz; Schoepfer, Joseph
PATENT ASSIGNEE(S): Ciba-Geigy A.-G., Switz.
SOURCE: PCT Int. Appl., 257 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9708193	A1	19970306	WO 1996-EP3473	19960806
W: AL, AU, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9667425	A1	19970319	AU 1996-67425	19960806
EP 846127	A1	19980610	EP 1996-927694	19960806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
ZA 9606967	A	19970217	ZA 1996-6967	19960816
PRIORITY APPLN. INFO.:			GB 1995-17060 A	19950817
			WO 1996-EP3473 W	19960806

OTHER SOURCE(S): MARPAT 126:264364
AB Peptides X-PTI-(AA)n-Y (AA = natural or unnatural amino acid residue, n = 0-15, PTI = tyrosine or preferably phosphotyrosine or phosphotyrosine mimic, X = arylcarbonyl, cycloalkylcarbonyl, tricycloalkylcarbonyl, arylsulfonyl, etc., Y = OH, C-terminal protecting group, amino group) or their salts were prepared for the treatment of diseases that respond to inhibition of the interaction of a protein comprising an SH2 domain and a protein tyrosine. Thus, 3-aminobenzyloxycarbonyl-Tyr(PO3H2)-Ile-Asn-Gln-NH2 trifluoroacetate salt was prepared by the solid phase method and had an IC50 value of 0.1 in a test system using the phosphorylated "tail" EGFR-MBP fusion protein as ligand. Formulations containing acylated oligopeptides are described.
IT **188749-93-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of acylated oligopeptide derivs. having cell signal inhibiting activity)
RN 188749-93-1 CAPLUS
CN L-Glutamamide, O-phosphono-N-(6-quinolinylcarbonyl)-L-tyrosyl-L-isoleucyl-L-asparaginyl- (9CI) (CA INDEX NAME)

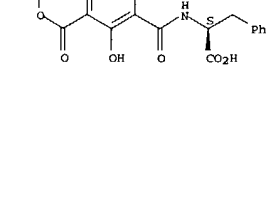
Absolute stereochemistry.

L4 ANSWER 222 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 223 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:277563 CAPLUS
DOCUMENT NUMBER: 126:289228
TITLE: Reduction of ochratoxin A toxicity by heat-induced epimerization. In vitro effects of ochratoxins on embryonic chick meningeal and other cell cultures
AUTHOR(S): Bruinink, A.; Rasonyi, T.; Sidler, C.
CORPORATE SOURCE: Inst. Toxicol., Swiss Fed. Inst. Technol., Univ. Zuerich, Schwerzenbach, CH-8603, Switz.
SOURCE: Toxicology (1997), 118(2,3), 205-210
CODEN: TXCYAC; ISSN: 0300-483X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study was designed to determine the toxic potential of three structurally related ochratoxins: ochratoxin A (OTA), ochratoxin B (OTB) and the heat-induced 3S-epimer of OTA (3S-OTA) recently discovered in roasted coffee and human serum. The toxicity was determined using serum-free cell cultures of embryonic chick meningeal fibroblasts, taking the effects on mitochondrial and lysosomal activity and culture protein content as an index for toxicity. OTA, OTB and 3S-OTA were toxic. However, the concentration
necessary to induce comparable effects were nearly 19- and 10-fold higher for OTB and 3S-OTA, resp., than those for OTA. In a next step and sensitivity of serum-free cell cultures of embryonic chick neural retina and brain were compared in relation to meningeal cell cultures. In the present study, no indications for differences in sensitivity could be detected. Furthermore, our study suggest that the OTA-induced toxic effects are not due to the inhibition by OTA of phenylalanine-tRNA synthetase.
IT **189152-21-4**
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(ochratoxin A toxicity in relation to structure)
RN 189152-21-4 CAPLUS
CN L-Phenylalanine, N-[[(3S)-5-chloro-3,4-dihydro-8-hydroxy-3-methyl-1-oxo-1H-2-benzopyran-7-yl]carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 224 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:207658 CAPLUS
DOCUMENT NUMBER: 126:199840
TITLE: Preparation of peptide derivatives as cell adhesion inhibitors
INVENTOR(S): Lin, Ko-Chung; Adams, Steven P.; Castro, Alfredo C.; Zimmerman, Craig N.; Cuervo, Julio Hernan; Lee, Wen-Cherng; Hammond, Charles E.; Carter, Mary Beth; Almquist, Ronald G.; Ensinger, Carol Lee
PATENT ASSIGNEE(S): Biogen, Inc., USA; Lin, Ko-Chung; Adams, Steven, P.; Castro, Alfredo, C.; Zimmerman, Craig, N.; Cuervo, Julio, Hernan; Lee, Wen-Cherng; Hammond, Charles, E.; Carter, Mary, Beth; et al.
SOURCE: PCT Int. Appl., 117 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9703094	A1	19970130	WO 1996-US11570	19960711
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
US 6248713	B1	20010619	US 1995-498237	19950711
CA 2226868	AA	19970130	CA 1996-2226868	19960711
AU 9664894	A1	19970210	AU 1996-64894	19960711
AU 716276	B2	20000224		
EP 842196	A1	19980520	EP 1996-924444	19960711
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI				
CN 1193325	A	19980916	CN 1996-196380	19960711
BR 9609782	A	19990309	BR 1996-9782	19960711
JP 11511124	T2	19990928	JP 1996-505989	19960711
NZ 312950	A	20000128	NZ 1996-312950	19960711
EE 3694	B1	20020415	EE 1997-362	19960711
EE 200200384	A	20021015	EE 2002-200200384	19960711
FI 9800033	A	19980305	FI 1998-33	19980109
NO 9800097	A	19980311	NO 1998-97	19980109
BG 63876	B1	20030430	BG 1998-102241	19980210
US 6239108	B1	20010529	US 1998-983391	19980810
US 6596687	B1	20030722	US 2000-482296	20000113
AU 758886	B2	20030403	AU 2000-36445	20000525
PRIORITY APPLN. INFO.:			US 1995-498237 A	19950711
			AU 1996-64894 A3	19960711
			WO 1996-US11570 W	19960711

OTHER SOURCE(S): MARPAT 126:199840
AB The present invention relates to novel peptide derivs. that are useful for inhibition and prevention of cell adhesion and cell adhesion-mediated pathologies. This invention also relates to pharmaceutical formulations comprising these compds. and methods of using them for inhibition and prevention of cell adhesion and cell adhesion-mediated pathologies. The compds. and pharmaceutical composition of this invention can be used as therapeutic or prophylactic agents. They are particularly well-suited for treatment of many inflammatory and autoimmune diseases. Thus, coupling of 4-(2-MeC6H4NHCONH)C6H4CH2CO2H (preparation given) with protected peptide

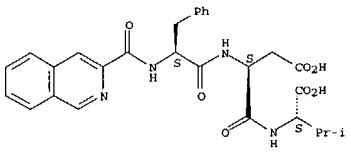
L4 ANSWER 224 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
H-Leu-Asp(OCH2Ph)-Val-OCH2Ph (prepn. given), followed by catalytic hydrogenolysis, gave cell adhesion inhibitor peptide 4-(2-MeC6H4NHCONH)C6H4CH2CO-Leu-Asp-Val-OH (I). All 408 prepd. peptide derivs., including I, inhibited VLA4-dependent adhesion to a bovine serum albumin conjugate with H-Cys-Tyr-Asp-Glu-Leu-Pro-Gln-Leu-Val-Thr-Leu-Pro-His-Pro-Asn-Leu-His-Gly-Pro-Glu-Ile-Leu-Asp-Val-Pro-Ser-Thr-OH, with IC50 values of <1 mM.

IT **187734-70-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptide derivs. as cell adhesion inhibitors)

RN 187734-70-9 CAPLUS

CN L-Valine, N-(3-isoquinolinylcarbonyl)-L-phenylalanyl-L-α-aspartyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 225 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:153973 CAPLUS

DOCUMENT NUMBER: 126:235990

TITLE: Transformation of the mycotoxin ochratoxin A in plants. 1. Isolation and identification of metabolites formed in cell suspension cultures of wheat and maize

AUTHOR(S): Ruhland, Monika; Engelhardt, Gabriele; Schaefer, Wolfram; Wallnoefer, Peter R.

CORPORATE SOURCE: Bayerische Landesanstalt fur Ernahrung, Abteilung Ernahrung, Munchen, 80638, Germany

SOURCE: Natural Toxins (1996), 4(6), 254-260
CODEN: NATOEE; ISSN: 1056-9014

PUBLISHER: Wiley-Liss

DOCUMENT TYPE: Journal

LANGUAGE: English

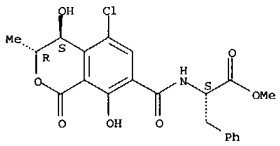
AB The metabolism of the mycotoxin ochratoxin A in plant cells was investigated by using cell suspension cultures of wheat and maize. A number of metabolites were detected by HPLC-chromatog. with fluorescence detection. The main metabolites were ochratoxin α, ochratoxin A Me ester, two isomers of hydroxyochratoxin A, and the glucosides and Me esters of both hydroxyochratoxin A isomers. The compds. were isolated by TLC and preparative HPLC and identified by mass spectrometry and specific enzymic reactions.

IT **188348-37-0**
RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(from transformation of ochratoxin A by suspension cultures of wheat and maize)

RN 188348-37-0 CAPLUS

CN L-Phenylalanine, N-[[(3R,4S)-5-chloro-3,4-dihydro-4,8-dihydroxy-3-methyl-1-oxo-1H-2-benzopyran-7-yl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 226 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:114532 CAPLUS

DOCUMENT NUMBER: 126:225198

TITLE: Combinatorial synthesis of heterocycles: solid phase synthesis of 2-arylquinoline-4-carboxylic acid derivatives

AUTHOR(S): Gopalsamy, Ariamala; Pallai, Peter V.

CORPORATE SOURCE: Department of Rational Drug Design, Procept, Inc., Cambridge, MA, 02139, USA

SOURCE: Tetrahedron Letters (1997), 38(6), 907-910
CODEN: TELEAY; ISSN: 0040-4039

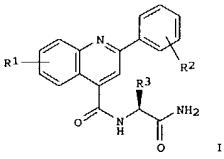
PUBLISHER: Elsevier

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 126:225198

GI



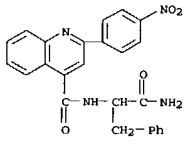
I

AB The Doebner quinoline synthesis has been adapted to solid phase. Acylation of an amino acid coupled to the Rink polystyrene resin with pyruvyl chloride afforded the immobilized amide. Further reaction of the amide with the preformed Schiff's base R1C6H4N:CHC6H4R2 (R1 = 3-MeO, R2 = 4-NO2, 4-cyano; R1 = H, R2 = 4-NO2) or aldehyde R2C6H4CHO and aniline R1C6H4NH2 gave, after trifluoroacetic acid cleavage, 2-arylquinoline-4-carboxylic acid amides I (R3 = H, CH2Ph, Me)in good yields.

IT **188367-36-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(solid phase synthesis of arylquinolinecarboxylic acid derivs.)

RN 188367-36-4 CAPLUS

CN 4-Quinolinecarboxamide, N-[2-amino-2-oxo-1-(phenylmethyl)ethyl]-5(or 7)-methoxy-2-(4-nitrophenyl)-, (S)- (9CI) (CA INDEX NAME)



D1—O—Me

L4 ANSWER 226 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

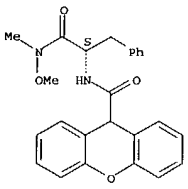
L4 ANSWER 227 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:113367 CAPLUS
DOCUMENT NUMBER: 126:122464
TITLE: Novel cathepsin Y and methods and compositions for inhibition thereof
INVENTOR(S): Tung, Jay S.; Sinha, Sukanto; Mcconlogue, Lisa; Tatsuno, Gwen; Anderson, John; Semko, Christopher M. F.; Chrysler, Susanna
PATENT ASSIGNEE(S): Athena Neurosciences, Inc., USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9639194	A1	19961212	WO 1996-US6211	19960426
W: CA, JP				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5783434	A	19980721	US 1995-467607	19950606
US 5849711	A	19981215	US 1995-469362	19950606
CA 2221684	AA	19961212	CA 1996-2221684	19960426
EP 831920	A1	19980401	EP 1996-913917	19960426
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11506923	T2	19990622	JP 1996-500507	19960426
US 5858982	A	19990112	US 1997-850392	19970502

PRIORITY APPLN. INFO.: US 1995-467607 19950606
US 1995-469362 19950606
WO 1996-US6211 19960426
OTHER SOURCE(S): MARPAT 126:122464
AB Methods for inhibiting the secretion of β-amyloid peptide (βAP) from cells comprise administering to the cells certain compds. which inhibit the activity of an approx. 31 kD protease involved in βAP secretion. The 31 kD protease has been designated Cathepsin Y. Screening methods for βAP inhibitors rely on determining the activity of test compds. in the presence of Cathepsin Y and a suitable peptide substrate. This invention is also directed to a nucleic acid sequence that encodes Cathepsin Y and the expression and isolation of Cathepsin Y.
IT **186030-84-2P**
RL: PNU (Preparation, unclassified); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(novel cathepsin Y and methods and compns. for inhibition thereof)
RN 186030-84-2 CAPLUS
CN 9H-Xanthene-9-carboxamide, N-[2-(methoxymethylamino)-2-oxo-1-(phenylmethyl)ethyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 227 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 228 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1997:113361 CAPLUS
DOCUMENT NUMBER: 126:117068
TITLE: Peptides and compounds that bind to the interleukin 1 (IL-1) receptor
INVENTOR(S): Barrett, Ronald W.; Yanofsky, Stephen D.; Baldwin, David; Jacobs, Jeff W.; Bovy, Philippe R.; Leahy, Ellen M.; Pottorf, Richard S.; Dharanipragada, Ramalinga; Tomlinson, Ronald C.
PATENT ASSIGNEE(S): Affymax Technologies N.V., UK; Barrett, Ronald W.; Yanofsky, Stephen D.; Baldwin, David; Jacobs, Jeff W.; Bovy, Philippe R.; Leahy, Ellen M.; Pottorf, Richard S.; Dharanipragada, Ramalinga; Tomlinson, Ronald C.
SOURCE: PCT Int. Appl., 73 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

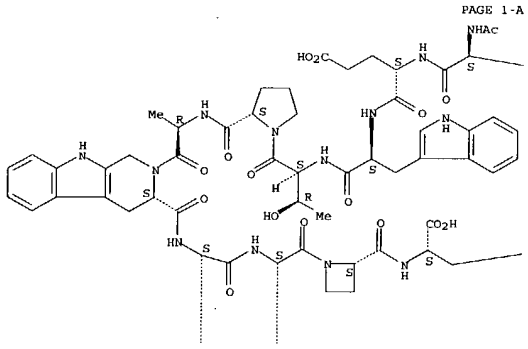
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9639165	A1	19961212	WO 1996-US9835	19960605
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA				
US 5861476	A	19990119	US 1995-464538	19950605
AU 9663820	A1	19961224	AU 1996-63820	19960605
EP 833654	A1	19980408	EP 1996-923258	19960605
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1995-464538 19950605
US 1994-190788 19940202
US 1995-383474 19950201
WO 1996-US9835 19960605
AB Peptides that bind to the interleukin-1 type I receptor (IL-1RtI) can be used to assay the amount of IL-1R, or an IL-1R agonist or antagonist that is useful for treatment of interleukin 1-mediated inflammatory responses or diseases to infection, tissue injury, rheumatoid arthritis, osteoarthritis, psoriasis, inflammatory bowel disease, encephalitis, glomerulonephritis and respiratory distress syndrome. Also provided are peptides which bind to the IL-1RtI, which are 11 to 40 amino acids in length.
IT **186251-93-4**
RL: ARU (Analytical role, unclassified); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(peptides and compds. that bind to the interleukin 1 receptor)
RN 186251-93-4 CAPLUS
CN L-Tyrosine, N-acetyl-L-phenylalanyl-L-α-glutamyl-L-tryptophyl-L-threonyl-L-prolyl-D-alanyl-(3S)-2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indole-3-carbonyl-L-tyrosyl-L-glutaminyl-(2S)-2-azetidinecarbonyl- (9CI) (CA INDEX NAME)

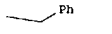
Absolute stereochemistry.

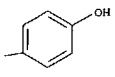
L4 ANSWER 228 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



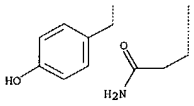
PAGE 1-B





L4 ANSWER 228 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A



L4 ANSWER 229 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:64014 CAPLUS
DOCUMENT NUMBER: 126:180811
TITLE: Inhibition of the cardiac sarcolemma Na+/Ca2+ exchanger by conformationally constrained small cyclic peptides
AUTHOR(S): Khananshvili, Daniel; Mester, Brenda; Saltoun, Miriam; Wang, Xiaolan; Shaulov, Gilat; Baazov, David
CORPORATE SOURCE: Department of physiology and Pharmacology, Sackler School of Medicine, Tel-Aviv University, Ramat-Aviv, 69978, Israel
SOURCE: Molecular Pharmacology (1997), 51(1), 126-131
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

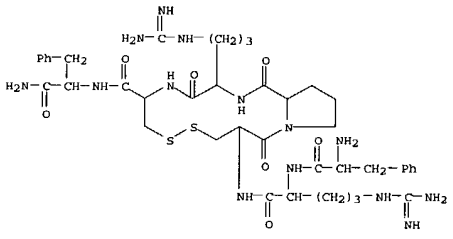
AB Pos. charged cyclic peptides (three to seven amino acids) have been tested for their inhibitory effects on Na+/Ca2+ exchange in the cardiac sarcolemma vesicles. The lead structure of Phe-Arg-Cys-Arg-Cys-Phe-CONH2 (FRCRCFa) has been systematically modified for identification of important pharmacophores. In cyclic peptides (intramol. S-S bond), the carboxyl terminal is locked with amide (CONH2), and pos. charge is retained by one or two arginines, ornithines, or lysines. Thirty-five different cyclic peptides show IC50 values in the range of 2-800 μM, suggesting that some specific structure-activity relationships may determine the inhibitory effects. Shortening of the FRCRCFa length to four amino acids decreases the inhibitory potency by 10-80-fold. The substitution of Arg2 or Arg4 in FRCRCFa with lysine or ornithine decreases the inhibitory potency by 5-12-fold, suggesting that both arginines are beneficial for inhibition. The substitution of Phe1 in FRCRCFa by 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid produces a potent inhibitor (IC50 = 2-4 μM). The N-myristoylated FRCRCFa exhibits an inhibitory potency (IC50 = 8-10 μM) similar to that of the parent FRCRCFa peptide, thereby arousing a new possibility for the development of a cell-permeable blocker of the Na+/Ca2+ exchanger. D-Arg4 or D-Cys5 substitutions in FRCRCFa do not alter the inhibitory effect, whereas the L-to-D substitutions of other amino acids in FRCRCFa reduce the inhibitory potency by 4-5-fold. Thus, the L-to-D substitutions of Arg4 and/or Cys5 have a potential to increase the peptide stability to proteolytic degradation The insertion of proline outside of the ring of FRCRCFa diminishes the inhibitory potency by 3-6-fold, whereas proline introduction into the ring decreases the inhibitory potency by 16-20-fold. The replacement of Cys3 and Cys5 in FRCRCFa with β,β-dimethylcystein has no significant effect on the inhibitory potency, suggesting that the S-S bond is not exposed to the interface of the peptide/receptor interaction. In conclusion, the current data support a proposal that the conformationally constrained Arg-Cys-Arg-Cys structure is obligatory for inhibition of Na+/Ca2+ exchange, whereas hydrophobic addns. at the carboxyl and amino ends have limited effects in increasing the inhibitory potency.

IT **187536-11-4P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(inhibition of cardiac sarcolemma Na+/Ca2+ exchanger by conformationally constrained small cyclic peptides in relation to structure)

RN 187536-11-4 CAPLUS

L4 ANSWER 229 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

CN L-Phenylalaninamide, L-phenylalanyl-L-arginyl-L-cysteinyl-L-prolyl-L-arginyl-L-cysteinyl-, cyclic (3→5)-disulfide (9CI) (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 230 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1997:16200 CAPLUS
DOCUMENT NUMBER: 126:99466
TITLE: Induction of histamine release from rat mast cells by bradykinin analogs
AUTHOR(S): Vietinghoff, Gabriele; Paegelow, Inge; Reissmann, Sigmund
CORPORATE SOURCE: Dep. Pharmacol. Toxicol., Univ. Rostock, Rostock, D-18055, Germany
SOURCE: Peptides (Tarrytown, New York) (1996), 17(8), 1467-1470
CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Independently of their agonistic or antagonistic activity on different isolated tissue prepns., the kinin analogs investigated induce histamine release on rat peritoneal mast cells. The effectivity of most compds. is 10 to 100 times higher than that of bradykinin. Beside the pos. charged amino acids, the elongation at the N-terminus with hydrophobic amino acids and the replacement of amino acids in the bradykinin sequence (especially at position 7) with aromatic residues is important for a high histamine-releasing activity.

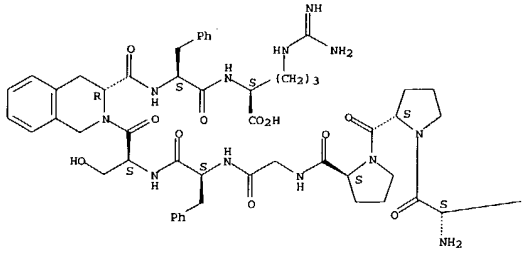
IT **183664-42-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(induction of histamine release from rat mast cells by bradykinin analogs)

RN 183664-42-8 CAPLUS

CN Bradykinin, 7-[(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid]- (9CI) (CA INDEX NAME)

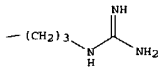
Absolute stereochemistry.

PAGE 1-A



L4 ANSWER 230 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

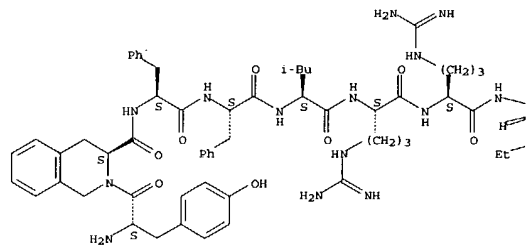
PAGE 1-B



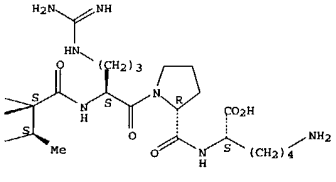
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 231 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



L4 ANSWER 231 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:696042 CAPLUS
DOCUMENT NUMBER: 126:26940
TITLE: The use of the message-address concept in the design of potential antagonists based on dynorphin A
AUTHOR(S): Kulkarni, S. N.; Choi, H.; Murray, T. F.; DeLander, G. E.; Aldrich, J. V.
CORPORATE SOURCE: College Pharmacy, Oregon State University, Corvallis, OR, 97331, USA
SOURCE: Peptides: Chemistry, Structure and Biology, Proceedings of the American Peptide Symposium, 14th, Columbus, Ohio, June 18-23, 1995 (1996), Meeting Date 1995, 655-656. Editor(s): Kaumaya, Pravin T. P.; Hodges, Robert S. Mayflower Scientific: Kingswinford, UK.
CODEN: 63NTAF
DOCUMENT TYPE: Conference
LANGUAGE: English

AB The authors used the message-address concept to design dynorphin A (Dyn A) analogs as potential opioid receptor antagonists by combining the message sequence from novel peptides reported to have δ and μ antagonist activity with the C-terminal address sequence of Dyn A (1-11). The affinities of the peptides for κ, δ, and μ receptors were evaluated in radioligand binding assays using [3H]DPDPE and [3H]DAMGO and cloned opioid receptors stably expressed in CHO cells. Opioid activity was evaluated in the elec. stimulated guinea pig ileum. Results indicated that incorporation of a modified message sequence into Dyn A analogs can affect opioid activity and that C-terminal address sequence of Dyn A can be used to significantly enhance κ opioid receptor affinity.

IT **184641-83-6P**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(opioid antagonist activity of peptides designed using message-address concept based on dynorphin A)

RN 184641-83-6 CAPLUS
CN 1-11-Dynorphin A (swine), 2-[(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid]-3-L-phenylalanine-10-D-proline- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 232 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:695907 CAPLUS
DOCUMENT NUMBER: 126:26919
TITLE: Conformational re-addressing of peptides towards interactions with other specific receptors
AUTHOR(S): Nikiforovich, G. V.; Kolodziej, S. A.; Zhang, W. -J.; Nock, B.; Bernad, N.; Martinez, J.; Marshall, G. R.
CORPORATE SOURCE: Center Molecular Design, Washington University, St. Louis, MO, 63130, USA
SOURCE: Peptides: Chemistry, Structure and Biology, Proceedings of the American Peptide Symposium, 14th, Columbus, Ohio, June 18-23, 1995 (1996), Meeting Date 1995, 346-347. Editor(s): Kaumaya, Pravin T. P.; Hodges, Robert S. Mayflower Scientific: Kingswinford, UK.
CODEN: 63NTAF
DOCUMENT TYPE: Conference
LANGUAGE: English

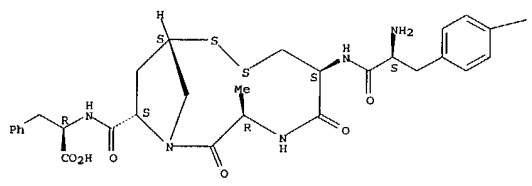
AB To induce potent and selective peptide-receptor interactions, "message" functional groups of a ligand should be spatially arranged to satisfy a specific 3D "address" of receptor. In this way, almost any peptide containing corresponding "message" elements could be modified to bind a receptor with known 3D "address". To demonstrate this, conformationally constrained analogs were designed starting from the sequences of cholecystokinin and angiotensin fragments (CCK-8, Asp-Tyr-Met-Gly-Trp-Met-Asp-Phe-NH2 and AT 4-8, Tyr-Val-His-Pro-Phe). The aim was to target δ-opioid receptor ("message" elements are shown in bold).

IT **184637-94-3**
RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(conformational re-addressing of peptides towards interactions with δ-opioid receptors)

RN 184637-94-3 CAPLUS
CN D-Phenylalanine, L-tyrosyl-D-cysteinyl-D-alanyl-(4S)-4-mercapto-L-prolyl-, cyclic (2→4)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

L4 ANSWER 232 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L4 ANSWER 233 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:686665 CAPLUS
DOCUMENT NUMBER: 126:54997
TITLE: Structure-activity studies of B1 receptor-related peptides: antagonists
AUTHOR(S): Gobeil, Fernand; Neugebauer, Withold; Filteau, Catherine; Jukic, Daniela; Allogho, Susanne Nsa; Pheng, Leng Hong; Nguyen-Le, Xuan Khai; Blouin, Daniel; Regoli, Domenico
CORPORATE SOURCE: Dept. of Pharmacology, Univ. de Sherbrooke Medical School, Sherbrooke, QC, J1H 5N4, Can.
SOURCE: Hypertension (Dallas) (1996), 28(5), 833-839
CODEN: HPRTDN; ISSN: 0194-911X
PUBLISHER: American Heart Association
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We tested several peptides related to des-Arg9-bradykinin as stimulants or inhibitors of B1 (rabbit aorta, human umbilical vein) and B2 (rabbit jugular vein, guinea pig ileum, human umbilical vein) receptors. We also incubated the compds. with purified angiotensin-converting enzyme from rabbit lung to test their resistance to degradation We evaluated apparent affinities (in terms of the affinity constant pA2) of compds. and their potential residual agonistic activities (αE). Bradykinin and des-Arg9-bradykinin were used as agonists for the B2 and B1 receptors, resp. Degradation of peptides by the angiotensin-converting enzyme was prevented in the presence of a D-residue in position 7 of des-Arg9-bradykinin. Replacement of Pro7 with D-Tic combined with Leu, Ile, Ala, or D-Tic in position 8 led to weak B1 receptor antagonists, some of which had strong residual agonistic activities on the B2 receptor prepns. The use of D-βNal in position 7, combined with Ile in position 8 and Ac-Lys at the N-terminal (e.g., Ac-Lys[D-βNal7,Ile8]des-Arg9-bradykinin) gave the most active B1 receptor antagonist (pA2 of 8.5 on rabbit aorta and human umbilical vein), which is also partially resistant to enzymic degradation Extension of the N-terminal end by Sar-Tyr-εAhx (used for labeling purposes) and even cold-labeling to Tyr with iodine were compatible with high, selective, and specific antagonism of the B1 receptors. We compared some compds. with some already known B1 receptor antagonists to underline the novelty of new peptidic compds.

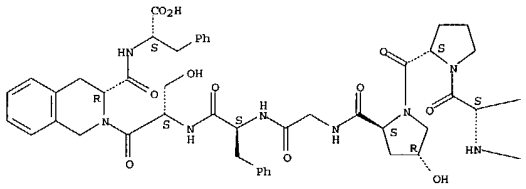
IT **185052-06-6**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(structure-activity studies of B1 receptor antagonist peptides)

RN 185052-06-6 CAPLUS
CN L-Phenylalanine, D-arginyl-L-arginyl-L-prolyl-(4R)-4-hydroxy-L-prolylglycyl-L-phenylalanyl-L-seryl-(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl- (9CI) (CA INDEX NAME)

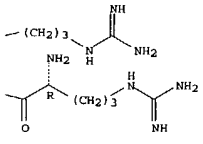
Absolute stereochemistry.

L4 ANSWER 233 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



L4 ANSWER 234 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:681493 CAPLUS
DOCUMENT NUMBER: 126:42242
TITLE: Development of Potent Thrombin Receptor Antagonist Peptides
AUTHOR(S): Bernatowicz, Michael S.; Klimas, Clifford E.; Hartl, Karen S.; Peluso, Marianne; Allegretto, Nick J.; Seiler, Steven M.
CORPORATE SOURCE: Bristol-Myers Squibb Pharmaceutical Research Institute, Princeton, NJ, 08543, USA
SOURCE: Journal of Medicinal Chemistry (1996), 39(25), 4879-4887
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

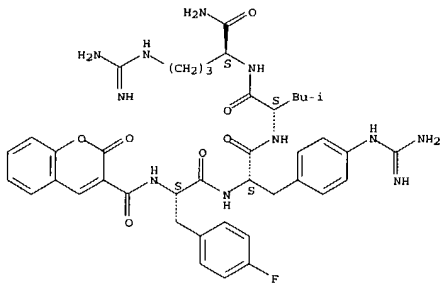
AB A peptide-based structure-activity study is reported leading to the discovery of novel potent thrombin receptor antagonists. Systematic substitution of nonproteogenic amino acids for the 2nd and 3rd residues of the human thrombin receptor tethered ligand sequence (SFLLR) led to a series of agonists with enhanced potency. The most potent pentapeptide agonist identified was Ser-p-fluoroPhe-p-guanidinoPhe-Leu-Arg-NH2 (I) (EC50 .apprx.0.04 μM for stimulation of human platelet aggregation, .apprx.10-fold more potent than the natural pentapeptide). Systematic substitution of the NH2-terminal Ser in I with neutral hydrophobic NH2-acyl groups led to partial agonists and eventually antagonists with unprecedented potency (>1000-fold increase over the previously reported antagonist 3-mercaptopropionyl-Phe-Cha-Cha-Arg-Lys-Pro-Asn-Asp-Lys-NH2). In the series of NH2-acyl tetrapeptide antagonists, N-trans-cinnamoyl-p-fluoroPhe-p-guanidinoPhe-Leu-Arg-NH2 (II) was identified as the tightest binding (IC50 .apprx.8 nM) and most potent with an IC50 .apprx.0.20 μM for inhibition of SFLLRNP-NH2-stimulated platelet aggregation. Systematic single substitutions in (II) indicated that, in addition to the NH2-terminal acyl group, the side chains at the 2nd and 3rd positions were also responsible for important and specific receptor interactions. The p-fluoroPhe and p-guanidinoPhe residues in the 2nd and 3rd positions of II were observed to be optimal in both the agonist and antagonist series. In the case of antagonists, however, an appropriately positioned pos. charged group (i.e., protonated base) at the 3rd residue was required. In contrast, such a substitution was not required for potent agonist activity. An even more potent antagonist resulted when II was extended at the C-terminus by a single Arg residue giving rise to analog BMS-200261 (III) which had an IC50 .apprx.20 nM for inhibition of SFLLRNP-NH2-stimulated platelet aggregation. When the C-terminal Arg of III was replaced by an Orn(Nδ-propionyl) residue, the resulting antagonist (BMS-200661) was suitable for use in radioligand binding assays (Kd = 10-30 nM). Antagonist activity observed for selected compds. was verified through secondary assays in that these analogs prevented SFLLRNP-NH2-stimulated GTPase activity in platelet membranes and Ca2+ mobilization in cultured human smooth muscle cells and mouse fibroblasts. Furthermore, this inhibition occurred at concns. that had no effect on thrombin catalytic activity, indicating a specific activity attributable to receptor binding and not enzyme inhibition.

IT **185028-23-3P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(development of potent thrombin receptor agonist and antagonist peptides)

RN 185028-23-3 CAPLUS
CN L-Argininamide, 4-fluoro-N-[(2-oxo-2H-1-benzopyran-3-yl)carbonyl]-L-

L4 ANSWER 234 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
phenylalanyl-4-[(aminoiminomethyl)amino]-L-phenylalanyl-L-leucyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 235 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

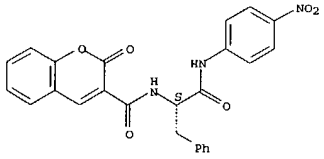
ACCESSION NUMBER: 1996:639677 CAPLUS
DOCUMENT NUMBER: 125:295746
TITLE: N-coumarinyl- or N-quinolinonyl peptide p-nitroanilides as intramolecularly quenched fluorogenic substrates
AUTHOR(S): Kokotos, G.; Charitos, C.; Tzougraki, C.
CORPORATE SOURCE: Department Chemistry, University Athens, Athens, GR-15771, Greece
SOURCE: Peptides 1994, Proceedings of the European Peptide Symposium, 23rd, Braga, Port., Sept. 4-10, 1994 (1995), Meeting Date 1994, 891-892. Editor(s): Maia, Hernani L. S. ESCOM: Leiden, Neth.
CODEN: 63MBAO
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Intramolecularly quenched fluorogenic substrates for proteases, i.e. a peptide chain bearing a fluorophore on one end and a quencher on the other, have been used for the determination of various proteases. The synthesis of four model substrates and studies on the quenching of fluorescence of aminocoumarin or aminoquinolinone-type fluorophores by the p-nitroanilide group are now reported for the assay of neutral endopeptidase-24.11.

IT **182944-07-6**
RL: ARG (Analytical reagent use); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process); USES (Uses)
(N-coumarinyl- or N-quinolinonyl peptide p-nitroanilides as intramolecularly quenched fluorogenic substrates)

RN 182944-07-6 CAPLUS
CN 2H-1-Benzopyran-3-carboxamide, N-[(1S)-2-[(4-nitrophenyl)amino]-2-oxo-1-(phenylmethyl)ethyl]-2-oxo- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 236 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:639551 CAPLUS
DOCUMENT NUMBER: 126:1294
TITLE: New linear and cyclic bradykinin agonists and antagonists
AUTHOR(S): Reissmann, S.; Pineda, L. F.; Seyfarth, L.; Greiner, G.; Schoelkens, B.; Vietinghoff, G.; Paegelow, I.
CORPORATE SOURCE: Institute Biochem. & Biophys, Friedrich-Schiller-University, Jena, D-07743, Germany
SOURCE: Peptides 1994, Proceedings of the European Peptide Symposium, 23rd, Braga, Port., Sept. 4-10, 1994 (1995), Meeting Date 1994, 619-620. Editor(s): Maia, Hernani L. S. ESCOM: Leiden, Neth.
CODEN: 63MBAO
DOCUMENT TYPE: Conference
LANGUAGE: English

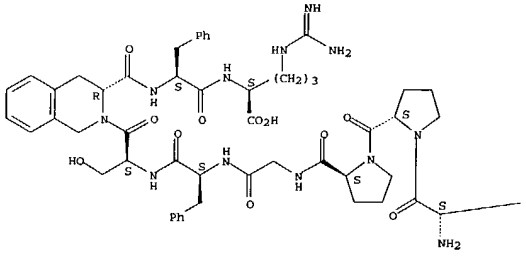
AB Despite the high potency of the bradykinin antagonist HOE-140 with the combination of D-Tic and Oic, unexpectedly D-Tic alone provides only a weak agonistic activity ([D-Tic7]BK RUT: 7.20%) and Oic alone leads to a poor antagonist ([Oic8]BK RUT: pA2 5.52). The combination of D-Tic with hydrophobic amino acids other than Oic is unable to give potent antagonists. The hydrophobic and constrained amino acid Oic at position 8 destroys the activity of potent agonists but enhances the antagonistic potencies of analogs with D-amino acids at position 7. Therefore, the authors conclude that in antagonists D-Tic can be replaced by other aromatic and non-aromatic amino acids, but Oic at position 8 is necessary for enhancement of the antagonistic activity. Beside the well known type of bradykinin antagonists with the key replacement at position 7 the authors could obtain two other types with amino acid replacements at positions 5 and 2.

IT **183664-42-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(new linear and cyclic bradykinin agonists and antagonists)

RN 183664-42-8 CAPLUS
CN Bradykinin, 7-[(3R)-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid]- (9CI) (CA INDEX NAME)

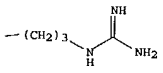
Absolute stereochemistry.

PAGE 1-A



L4 ANSWER 236 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-B



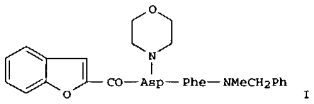
L4 ANSWER 237 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:494173 CAPLUS
DOCUMENT NUMBER: 125:143330
TITLE: Peptide compounds for prevention and/or treatment of nitric oxide (NO)-mediated diseases
INVENTOR(S): Itoh, Yoshikuni; Iwamoto, Toshiro; Yatabe, Takumi; Hamashima, Hitoshi; Inoue, Takayuki; Hashimoto, Seiji; Oku, Teruo
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 739 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9616981	A2	19960606	WO 1995-JP2428	19951129
WO 9616981	A3	19960906		
W: AU, CA, CN, FI, HU, JP, KR, MX, NO, NZ, RU, UA, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9539937	A1	19960619	AU 1995-39937	19951129
EP 796270	A2	19970924	EP 1995-938602	19951129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
ZA 9510201	A	19960625	ZA 1995-10201	19951130
US 5932737	A	19990803	US 1997-849076	19970530

PRIORITY APPLN. INFO.: GB 1994-24408 A 19941202
GB 1995-4891 A 19950310
GB 1995-10042 A 19950518
WO 1995-JP2428 W 19951129

OTHER SOURCE(S): MARPAT 125:143330
GI



I

AB Peptides WA1NR8CH(A2T)CONR9CH(A3R3)R4 [W = alkyl, (un)substituted aryl or fluorenyl, etc.; A1 = alkylene, NHCO, CO, CS, SO2; A2 = alkylene; T = H, aryl, heterocyclyl, OH, etc.; R8 = H, alkyl; R8 may link with A2T to form CH2C6H4CH2-o (Q); A3 = bond, alkylene; R3 = H, aryl, OH, etc.; R9 = H, alkyl or may link with A3R3 to form Q; R4 = CO2H, protected carboxy, carboxamido, etc. or CH(A3R3)R4 = N-alkyl-2-oxoquinoline moiety] or their pharmaceutically acceptable salts were prepared for use as medicaments. Thus, dipeptide I was prepared by acylation of aspartylphenylalaninamide derivative with 2-benzofurancarboxylic acid. I and six other peptides showed

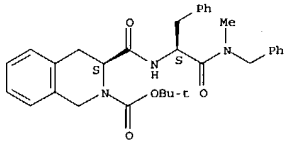
L4 ANSWER 237 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

100% inhibition of NO prodn. in tests of murine macrophage cells.

IT **179875-74-2P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of peptides for prevention and/or treatment of nitric oxide-mediated diseases)

RN 179875-74-2 CAPLUS
CN 2(1H)-Isoquinolinecarboxylic acid, 3,4-dihydro-3-[[[2-[methyl(phenylmethyl)amino]-2-oxo-1-(phenylmethyl)ethyl]amino]carbonyl]-, 1,1-dimethylethyl ester, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 238 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:466915 CAPLUS
DOCUMENT NUMBER: 125:143315
TITLE: Boronic ester and acid compounds, synthesis and uses
INVENTOR(S): Adams, Julian; Ma, Yu-Ting; Stein, Ross; Baevsky, Matthew; Grenier, Louis; Plamondon, Louis
PATENT ASSIGNEE(S): Proscript, Inc., USA
SOURCE: PCT Int. Appl., 144 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9613266	A1	19960509	WO 1995-US14117	19951027
W: AL, AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6083903	A	20000704	US 1995-442581	19950516
AU 9641398	A1	19960523	AU 1996-41398	19951027
AU 710564	B2	19990923		
EP 788360	A1	19970813	EP 1995-939670	19951027
EP 788360	B1	20030528		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10510245	T2	19981006	JP 1995-514834	19951027
AT 241631	E	20030615	AT 1995-939670	19951027
FI 9701746	A	19970606	FI 1997-1746	19970423
NO 9701929	A	19970612	NO 1997-1929	19970425

PRIORITY APPLN. INFO.: US 1994-330525 A 19941028
US 1995-442581 A 19950516
WO 1995-US14117 W 19951027

OTHER SOURCE(S): MARPAT 125:143315

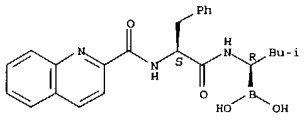
AB Peptidyl boronic acids and esters PNR[B1R1X1]ACHR2X2CHR3BZ1Z2 [P = aryl-, aralkyl-, heteroaryl-, or heteroarylalkylcarbonyl or -sulfonyl; B1 = N, CH; X1, X2 = CONH, CH(OH)CH2, COCH2; A = 0, 1, 2; R = H, alkyl; RR1 or RR2 (for A = 0) may form a ring; R1, R2, R3 = H, alkyl, cycloalkyl, aryl, etc.; Z1, Z2 = alkyl, hydroxy, alkoxy, aryloxy; Z1Z2 may form a moiety derived from a dihydroxy compound] and their pharmaceutically acceptable salts were prepared The rate of degradation of proteins of an animal can be reduced by contacting cells of the animal with these boronic compds. Thus, N-(4-morpholinecarbonyl)-β-(1-naphthyl)-L-alanine-L-leucine boronic acid was prepared by coupling (1S,2S,3R,5S)-pinanediol leucine boronate trifluoroacetate salt with N-Boc-β-(1-naphthyl)-L-alanine, followed by deprotection, acylation with 4-morpholinecarbonyl chloride, and cleavage of the pinanediol moiety.

IT **179324-53-9**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(synthesis of peptidyl boronic acids and esters as proteolytic enzyme inhibitors)

RN 179324-53-9 CAPLUS
CN Boronic acid, [(1R)-3-methyl-1-[[(2S)-1-oxo-3-phenyl-2-[(2-quinolinylcarbonyl)amino]propyl]amino]butyl]- (9CI) (CA INDEX NAME)

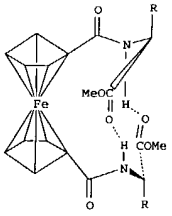
Absolute stereochemistry.

L4 ANSWER 238 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 239 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:457338 CAPLUS
DOCUMENT NUMBER: 125:248351
TITLE: Ordered conformations in bis(amino acid) derivatives of 1,1'-ferrocenedicarboxylic acid
AUTHOR(S): Herrick, Richard S.; Jarret, Ronald M.; Curran, Timothy P.; Dragoli, Dean R.; Flaherty, Maryellen B.; Lindyberg, Susan E.; Slate, Rebecca A.; Thornton, Lisa C.
CORPORATE SOURCE: Dep. Chem., Coll. Holy Cross, Worcester, MA, 01610, USA
SOURCE: Tetrahedron Letters (1996), 37(30), 5289-5292
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



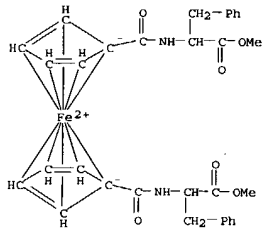
I

AB Two bis(amino acid) derivs. I (R = Me2CH, PhCH2) of 1,1'-ferrocenedicarboxylic acid were characterized by IR, 1H NMR and 13C NMR spectroscopy. Each was found to adopt an ordered, intramolecularly H bonded conformation in CHCl3.

IT **181589-78-6P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(ordered conformations in bis(amino acid) derivs. of ferrocenedicarboxylic acid)

RN 181589-78-6 CAPLUS
CN Ferrocene, 1,1'-bis[[[(1S)-2-methoxy-2-oxo-1-(phenylmethyl)ethyl]amino]carbonyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 239 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

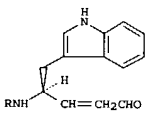


L4 ANSWER 240 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:443908 CAPLUS
DOCUMENT NUMBER: 125:115147
TITLE: Preparation of peptide aldehyde derivatives as cysteine protease inhibitors
INVENTOR(S): Sohda, Takashi; Fujisawa, Yukio; Yasuma, Tsuneo; Mizoguchi, Junji
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: PCT Int. Appl., 85 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9610014	A1	19960404	WO 1995-JP1933	19950925
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, US, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2196182	AA	19960404	CA 1995-2196182	19950925
AU 9535341	A1	19960419	AU 1995-35341	19950925
JP 08151355	A2	19960611	JP 1995-245957	19950925
EP 783489	A1	19970716	EP 1995-932228	19950925
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				

PRIORITY APPLN. INFO.: JP 1994-231839 19940927
WO 1995-JP1933 19950925
OTHER SOURCE(S): MARPAT 125:115147
GI



I

AB The present invention relates to acylaminoaldehyde compds. of formula R4-Q-NHCHR1-X-CHO (Q = one or two amino acid residual groups which may be substituted; R1 = hydrogen atom or an optionally substituted hydrocarbon or heterocyclic group; R4 = an optionally esterified carboxyl group or an acyl group; X = a optionally substituted straight-chain or branched divalent hydrocarbon group having a chain length of 1 to 4 atoms as the linear moiety], or salts thereof, which have strong cysteine protease inhibitory activities and are useful as prophylactic and therapeutic agent of various diseases, including bone diseases, caused by abnormal exasperation of cystine protease, are prepared. Thus, 2.4 g N-tert-butoxycarbonyl-L-phenylalanyl-L-tryptophanal and 1.76 g (formylmethylene)triphenylphosphorane were dissolved in 10 mL THF and 30 mL toluene and stirred for 15 h to give the title compound (I; R = Boc-Phe).

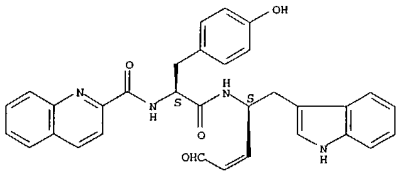
L4 ANSWER 240 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

The latter compd. and I (R = PhCH2O2C-Leu-Leu) (II) in vitro showed IC50 of 3.5 + 10-8 and 9.7 + 10-9 M, resp., against cathepsin L and that of 2.4 + 10-6 and 9.7 + 10-7 M, resp., against cathepsin B, resp. In a bone resorption inhibitory assay, they in vitro inhibited by 83 and 51%, resp., the Ca release from fetal rat's forearm bones. A gelatin capsule formulation contg. II was described.

IT **178910-81-1P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptide aldehyde derivs. as cysteine protease inhibitors and bone resorption inhibitors for treating bone diseases)

RN 178910-81-1 CAPLUS
CN 2-Quinolinecarboxamide, N-[1-[(4-hydroxyphenyl)methyl]-2-[[1-(1H-indol-3-ylmethyl)-4-oxo-2-butenyl]amino]-2-oxoethyl]-, [S-(R*,R*)]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.



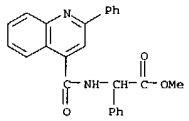
L4 ANSWER 241 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:393848 CAPLUS
DOCUMENT NUMBER: 125:25636
TITLE: 2-Phenyl-4-quinolinecarboxamides: A Novel Class of Potent and Selective Non-Peptide Competitive Antagonists for the Human Neurokinin-3 Receptor
AUTHOR(S): Giardina, Giuseppe A. M.; Sarau, Henry M.; Farina, Carlo; Medhurst, Andrew D.; Grugni, Mario; Foley, James J.; Raveglia, Luca F.; Schmidt, Dulcie B.; Rigolio, Roberto; et al.
CORPORATE SOURCE: Department of Chemistry, SmithKline Beecham S.p.A., Baranzate, 20021, Italy
SOURCE: Journal of Medicinal Chemistry (1996), 39(12), 2281-2284
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A novel class of potent and selective, non-peptide NK-3 receptor antagonists, based on the 2-phenylquinoline framework, has been identified and characterized by binding anal. using membrane preparation of CHO cells expressing the human neurokinin receptors (hNKs-CHO). Functional activity was determined by inhibition of senktide-induced contraction of the rabbit isolated iris sphincter muscle preparation An extensive structure-activity study led to the identification of (S)-(-)-N-(α-ethylbenzyl)-3-hydroxy-2-phenylquinoline-4-carboxamide (SB 223412) as the most potent (Ki = 1.0 nm in hNK-3-CHO binding; Kb = 5.4 nM for antagonism of senktide-induced contraction in rabbit iris sphincter muscle) and selective (hNK-2/hNK-3 Ki ratio of 144 and hNK-1/hNK-3 Ki ratio > 100,000) hNK-3 receptor antagonist of this class. In addition, NKB-induced Ca2+ mobilization studies in hNK-3-HEK 293 cells indicated that SB 223412 is a reversible, competitive antagonist. Compds. from this novel class will be extremely useful in the functional characterization of hNK-3 receptors and elucidation of potential therapeutic indications for selective hNK-3 receptor antagonists.

IT **174635-51-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation and structure-activity of human neurokinin 3 receptor antagonists phenylquinolinecarboxamides)

RN 174635-51-9 CAPLUS
CN Benzeneacetic acid, α-[[(2-phenyl-4-quinolinyl)carbonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)



L4 ANSWER 241 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L4 ANSWER 242 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

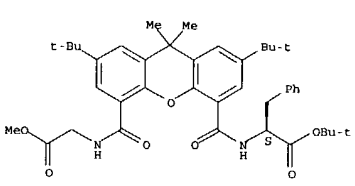
ACCESSION NUMBER: 1996:367060 CAPLUS
DOCUMENT NUMBER: 125:81189
TITLE: Application of capillary electrophoresis-electrospray ionization mass spectrometry in the determination of molecular diversity
AUTHOR(S): Dunayevskiy, Yuriy M.; Vouros, Paul; Wintner, Edward A.; Shipps, Gerald W.; Carell, Thomas; Rebek, Julius, Jr.
CORPORATE SOURCE: Dep. Chem., Northeastern Univ., Boston, MA, 02115, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1996), 93(12), 6152-6157
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English

AB By capillary electrophoresis coupled online to electrospray ionization MS, a library of theor. 171 distributed xanthene derivs. was analyzed. The method allowed the purity and makeup of the library to be determined: 160 of the expected compds. were found to be present, and 12 side-products were also detected in the mixture Due to the ability of capillary electrophoresis to sep. analytes on the basis of charge, most of the xanthene derivs. could be resolved by simple capillary electrophoresis-MS procedures even though 124 of the 171 theor. compds. were isobaric with ≥1 other mol. in the mixture Any remaining unresolved peaks were resolved by MS/MS expts. The method shows promise for the anal. of small combinatorial libraries with <1000 components.

IT **178916-07-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(application of capillary electrophoresis-electrospray ionization mass spectrometry in determination of mol. diversity of xanthene derivs.)

RN 178916-07-9 CAPLUS
CN L-Phenylalanine, N-[[2,7-bis(1,1-dimethylethyl)-5-[[(2-methoxy-2-oxoethyl)amino]carbonyl]-9,9-dimethyl-9H-xanthen-4-yl]carbonyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 243 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:366713 CAPLUS
DOCUMENT NUMBER: 125:76666
TITLE: Modification of the C-terminal dipeptide of angiotensin II yielded a novel series of analogs with II (AT2) receptor selectivity
AUTHOR(S): Cody, Wayne L.; He, John X.; Lunney, Elizabeth A.; Humblet, Christine C.; Lu, Gina H.; Panek, Robert L.; Dudley, David T.
CORPORATE SOURCE: Department Chemistry, Parke-Davis Pharmaceutical Research, Ann Arbor, MI, 48105, USA
SOURCE: Protein and Peptide Letters (1996), 3(2), 107-112
CODEN: PPELEN; ISSN: 0929-8665
PUBLISHER: Bentham Science Publishers BV
DOCUMENT TYPE: Journal
LANGUAGE: English

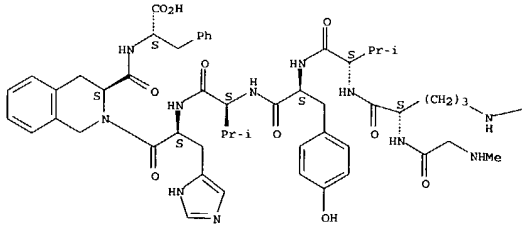
AB Angiotensin II is a potent pressor agent acting through two distinct G-protein coupled receptors. The type I (AT1) receptor is responsible for the pressor activity while the function of the type II (AT2) receptor remains unclear. Specific modifications of the C-terminal dipeptide (-Pro7-Phe8) of angiotensin II with constrained aromatic (Tic) and hydrophobic (Oic) amino acids have led to analogs with negligible affinity for the AT1 receptor, but nanomolar affinity for the AT2 receptor. These compds. may provide useful tools to help delineate the physiol. role of the AT2 receptor.

IT **178403-48-0**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(modification of C-terminal dipeptide of angiotensin II yielded series of analogs AT2 receptor selectivity)

RN 178403-48-0 CAPLUS
CN Angiotensin II, 1-(N-methylglycine)-5-L-valine-7-(L-1,2,3,4-tetrahydro-3-isoquinolinecarboxylic acid)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



L4 ANSWER 243 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

L4 ANSWER 244 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:353996 CAPLUS
DOCUMENT NUMBER: 125:1605
TITLE: Novel Cyclic Analogs of Angiotensin II with Cyclization between Positions 5 and 7: Conformational and Biological Implications
AUTHOR(S): Zhang, Wei-Jun; Nikiforovich, Gregory V.; Perodin, Jacqueline; Richard, Darren E.; Escher, Emanuel; Marshall, Garland R.
CORPORATE SOURCE: Department of Molecular Biology and Pharmacology, Washington University, St. Louis, MO, 63130, USA
SOURCE: Journal of Medicinal Chemistry (1996), 39(14), 2738-2744
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

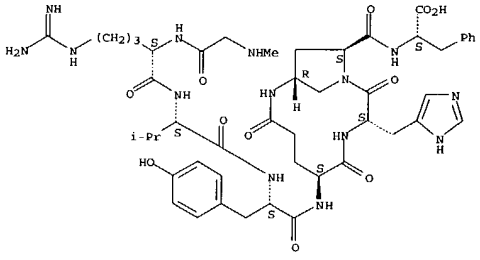
AB To study the conformational features of mol. recognition of angiotensin II (Asp1-Arg2-Val3-Tyr4-Val/Ile5-His6-Pro7-Phe8, AII), the synthesis and biol. testing of several cyclic analogs of AII cyclized between positions 5 and 7 have been performed. The synthesized analogs were Sar1-Arg2-Val3-Tyr4-cyclo(Cys5-His6-Pen7)-Phe8 (3), Sar1-Arg2-Val3-Tyr4-cyclo(Asp5-His6-Apt7)-Phe8 (4), Sar1-Arg2-Val3-Tyr4-cyclo(Glu5-His6-Apt7)-Phe8 (5), Sar1-Arg2-Val3-Tyr4-cyclo(Cys5-His6-Mpt7)-Phe8 (6), Sar1-Arg2-Val3-Tyr4-cyclo(Cys5-His6-Mpc7)-Phe8 (7), Sar1-Arg2-Val3-Tyr4-cyclo(Hcy5-His6-Mpt7)-Phe8 (8), and Sar1-Arg2-Val3-Tyr4-cyclo(Hcy5-His6-Mpc7)-Phe8 (9), where Apt stands for 4-amino-trans-proline, and Mpt and Mpc for 4-mercapto-trans- and -cis-prolines, resp. Compound (9) showed good affinity at AT-1 receptors, namely a KD = 20 nM. In functional assays, it showed the characteristics of a weak partial agonist with a relative affinity of 0.26% of that for AII and an intrinsic efficacy, αE, of 0.42. Mol. modeling suggested a possible explanation for this finding: the relatively strong binding and the weak partial agonistic activity of compound 9 are due to interaction with AT-1 receptor of only two functionally important groups, namely, the side chains of the His6 and Phe8 residues.

IT **177480-67-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(conformational and biol. implications of novel cyclic analogs of angiotensin II with cyclization between positions 5 and 7)

RN 177480-67-0 CAPLUS
CN L-Phenylalanine, N-methylglycyl-L-arginyl-L-valyl-L-tyrosyl-L-α-glutamyl-L-histidyl-trans-4-amino-L-prolyl-, cyclic (5→7)-peptide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 244 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



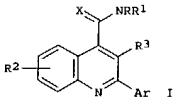
L4 ANSWER 245 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:341820 CAPLUS
DOCUMENT NUMBER: 125:33490
TITLE: Preparation of quinoline-4-carboxamides and related compounds as as NK3 antagonists.
INVENTOR(S): Farina, Carlo; Giardina, Giuseppe Arnaldo Mari; Grugni, Mario; Raveglia, Luca Francesco
PATENT ASSIGNEE(S): Smithkline Beecham Farmaceutici S.P.A., Italy
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9602509	A1	19960201	WO 1995-EP2638	19950706

W: JP, US
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRIORITY APPLN. INFO.: IT 1994-MI1466 19940714
OTHER SOURCE(S): MARPAT 125:33490
GI

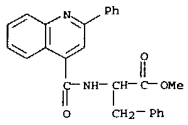


AB Title compds. [I; Ar = (substituted) Ph, naphthyl, heterocyclyl; R = (substituted) Ph, heterocyclyl, CHR4R5; R4 = H, alkyl, cycloalkyl, (substituted) Ph, heteroaryl, etc.; R5 = alkyl, (CH2)nAr; n = 0-3; R1 = H, alkyl; R2, R3 = H, alkyl, alkenyl, aryl, carboxamido, sulfonamido, alkoxy, OH, halo, NO2, cyano, hydroxyalkyl, aminoalkyl, acylamino, CO2H, alkylsulfonylamino, etc; X = O, S, H2, NCN], were prepared Thus, benzylamine, 2-phenylquinoline-4-carbonyl chloride, and K2CO3 were stirred in DMF at 0°-room temperature overnight to give N-benzyl-2-phenylquinoline-4-carboxamide. The latter inhibited binding of 125I-N-Me-Phe7-NKB to guinea pig cortical membranes with IC50 = 620 nM.

IT **189815-92-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinoline-4-carboxamides and related compds. as as NK3 antagonists)

RN 189815-92-7 CAPLUS
CN Phenylalanine, N-[(2-phenyl-4-quinolinyl)carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

L4 ANSWER 245 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 246 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

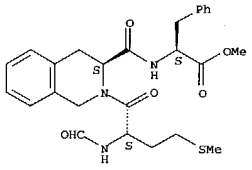
ACCESSION NUMBER: 1996:339994 CAPLUS
DOCUMENT NUMBER: 125:56105
TITLE: The importance of the peptide bond at position 2 in HCO-Met-Leu-Phe-OMe analogs as shown by studies on human neutrophils
AUTHOR(S): Cavicchioni, Giorgio; Breveglieri, Angela; Boggian, Marisa; Vertuani, Gianni; Reali, Eva; Spisani, Susanna
CORPORATE SOURCE: Department Pharmaceutical Sciences, University Ferrara, Ferrara, Italy
SOURCE: Journal of Peptide Science (1996), 2(3), 135-140
CODEN: JPSIEI; ISSN: 1075-2617
PUBLISHER: Wiley
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The formylpeptides formyl-methionyl-N-methylleucyl-phenylalanine Me ester [for-Met-(NMe)Leu-Phe-OMe], formyl-methionyl-2-aminotetralin-2-carboxyl-phenylalanine Me ester [for-Met-Atc-Phe-OMe] 2, formyl-methionyl-1,2,3,4-tetrahydroisoquinoline-3-carboxyl-phenylalanine Me ester [for-Met-Tic-Phe-OMe] and formyl-methionyl-2-aminoxy-4-methylvalerly-phenylalanine Me ester [for-Met-OLeu-Phe-OMe] were synthesized in order to investigate the role of the amide bond at position 2 on biol. activities on human neutrophils. Only analog 2, which keeps the NH group at position 2, was found to retain biol. activity for neutrophils (chemotaxis, superoxide formation, and lysozyme release), though sterically encumbered.

IT **177656-62-1**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amide bond of formyl-Met-Leu-Phe peptide analogs is important for chemotactic activity toward neutrophils)

RN 177656-62-1 CAPLUS
CN L-Phenylalanine, N-[[(3S)-2-[(2S)-2-(formylamino)-4-(methylthio)-1-oxobutyl]-1,2,3,4-tetrahydro-3-isoquinolinyl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 247 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

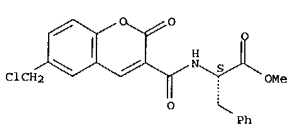
ACCESSION NUMBER: 1996:328195 CAPLUS
DOCUMENT NUMBER: 125:323
TITLE: Esters and Amides of 6-(Chloromethyl)-2-oxo-2H-1-benzopyran-3-carboxylic Acid as Inhibitors of α-Chymotrypsin: Significance of the "Aromatic" Nature of the Novel Ester-Type Coumarin for Strong Inhibitory Activity
AUTHOR(S): Pochet, Lionel; Doucet, Caroline; Schynts, Marc; Thierry, Nicole; Boggetto, Nicole; Pirotte, Bernard; Jiang, Kai Y.; Masereel, Bernard; de Tullio, Pascal; et al.
CORPORATE SOURCE: Laboratoire de Chimie Pharmaceutique, Universite de Liege, Liege, B-4000, Belg.
SOURCE: Journal of Medicinal Chemistry (1996), 39(13), 2579-2585
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A series of esters and amides of 6-(chloromethyl)-2-oxo-2H-1-benzopyran-3-carboxylic acid were synthesized and evaluated in vitro for their inhibitory activity toward bovine α-chymotrypsin and human leukocyte elastase. Both series behaved as time-dependent inhibitors of α-chymotrypsin, but ester-type coumarins were clearly more efficient than the corresponding amides in inactivating the serine proteinase. The best inactivation was observed with "aromatic" esters, in particular with meta-substituted Ph esters such as m-chlorophenyl 6-(chloromethyl)-2-oxo-2H-1-benzopyran-3-carboxylate, which appears to be one of the most powerful inactivators of α-chymotrypsin yet reported (kinact/KI = 760 000 M-1 s-1 at pH 7.5 and 25°). Usually, the coumarin deriva. failed to inhibit significantly human leukocyte elastase. As a result, the reported series of aromatic coumarinic esters behaves as a new chemical family of selective α-chymotrypsin inhibitors.

IT **176770-52-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of esters and amides of 6-(chloromethyl)-2-oxo-2H-1-benzopyran-3-carboxylic acid as inhibitors of α-chymotrypsin)

RN 176770-52-8 CAPLUS
CN L-Phenylalanine, N-[[6-(chloromethyl)-2-oxo-2H-1-benzopyran-3-yl]carbonyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 248 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:313253 CAPLUS
DOCUMENT NUMBER: 125:80883
TITLE: Isolation and identification of peptide conformers by reversed-phase high-performance liquid chromatography and NMR at low temperature
AUTHOR(S): Kalman, Andras; Thunecke, Frank; Schmidt, Ralf; Schiller, Peter W.; Horvath, Csaba
CORPORATE SOURCE: Department of Chemical Engineering, Yale University, P.O. Box 208286, New Haven, CT, 06520-8286, USA
SOURCE: Journal of Chromatography, A (1996), 729(1 + 2), 155-171
CODEN: JCRAEY; ISSN: 0021-9673
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

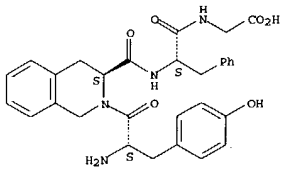
AB Peptide conformers with one or more rotationally hindered peptide bonds due to the presence of proline and/or another N-substituted amino acid residue in the mol. were separated by reversed-phase chromatog. at low temps., isolated and identified by NMR. The scope of this investigation included the cis-trans isomers of the dipeptides as Leu-Pro, Phe-Pro and Tyr-Pro as well as conformers of opioid peptides containing proline and/or the proline-like Tic (1,2,3,4-tetrahydro-isoquinoline-3-carboxylic acid) residues: Tyr-Pro-Phe (β-casomorphin 1-3 fragment), Tyr-Tic-Phe-Phe, Tyr-Pro-Phe-Pro-Gly (β-casomorphin-5), Tyr-Tic-Phe-Phe-Val-Val-Gly-NH2 and Tyr-Tic-Phe-Gly-Tyr-Pro-Ser-NH2. Chromatog. with micropellicular and totally porous octadecylated silica stationary phases and aqueous methanol under isocratic elution conditions resulted in well separated peaks of the rotational isomers at sufficiently low temps. Preparative RP-HPLC was carried out with eluents containing water and methanol, both deuterated, and the effluent fractions containing each isomer were collected for further investigation. The conformational states of the peptide isomers upon separation were conserved by storing the effluent fractions in liquid nitrogen. The Leu-Pro, Phe-Pro, Tyr-Pro and Tyr-Pro-Phe conformers were identified by one- and two-dimensional NMR spectroscopy at -15°C. Upon comparing the NMR spectra of the isomers, for these peptides the retention order of the conformers was unambiguously established: in each case the trans conformer is eluted before the cis conformer. On the basis of NMR data obtained with β-casomorphin-5, which contains 2 proline residues, the elution order of its 4 conformers was established by NMR spectroscopy of the fractions obtained by RP-HPLC at low temperature as trans-trans (least retained), trans-cis, cis-cis and cis-trans (most retained).

IT **178748-31-7**
RL: ANT (Analyte); PRP (Properties); ANST (Analytical study)
(identification of peptide conformers by reversed-phase HPLC and NMR)

RN 178748-31-7 CAPLUS
CN Glycine, L-tyrosyl-L-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 248 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

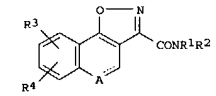


L4 ANSWER 249 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

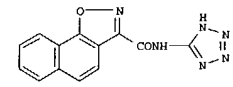
ACCESSION NUMBER: 1996:290583 CAPLUS
DOCUMENT NUMBER: 124:343279
TITLE: Preparation of naphth[2,1-d]isoxazole-3-carboxamide derivatives as antiulcer drugs
INVENTOR(S): Hasegawa, Yukio; Sato, Michitaka; Hasumi, Koichi; Yamamoto, Norio; Matsui, Teruaki; Shidara, Kazuhiro; Kenjo, Takashi; Myazawa, Katsuhiko; Ogawa, Chisato; Et, Al.
PATENT ASSIGNEE(S): Teikoku Hormone Mfg Co Ltd, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 20 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08027131	A2	19960130	JP 1994-180457	19940711

PRIORITY APPLN. INFO.: JP 1994-180457 19940711
OTHER SOURCE(S): MARPAT 124:343279
GI



I



II

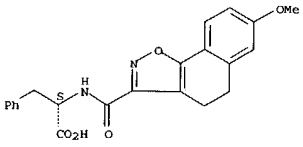
AB Naphthisoxazole derivs. [I; A = CH, CH2, S, O, SO2; R1 = H, alkyl; R2 = hydroxyalkyl, alkoxyalkyl, heterocyclyl containing 1-4 heteroatoms selected from N, S, and O; n = 2-5; R1R2N = heterocyclyl; R3, R4 = H, halo, alkyl, alkoxy, alkenyloxy, OH; when A is CH or CH2, R1 is H] and their salts are prepared for use as antiulcer drugs. Thus, 3-carboxynaphth[2,1-d]isoxazole was treated with PCl5 and then reacted with 5-amino-1H-tetrazole to give 3-(1H-tetrazol-5-ylcarbamoyl)naphth[2,1-d]ixoxazole (II), which inhibited stress-induced ulcer at 30 mg/kg oral in male rats.

IT **176432-23-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of naphth[2,1-d]isoxazole-3-carboxamide derivs. as antiulcer drugs)

L4 ANSWER 249 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

RN 176432-23-8 CAPLUS
CN L-Phenylalanine, N-[(4,5-dihydro-7-methoxynaphth[2,1-d]isoxazol-3-yl)carbonyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 250 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

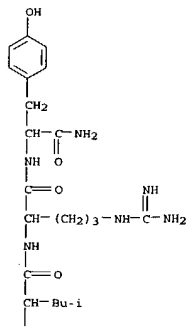
ACCESSION NUMBER: 1996:257145 CAPLUS
DOCUMENT NUMBER: 125:34134
TITLE: Synthesis, structure and stability of novel dimeric peptide-disulfides
AUTHOR(S): Leban, Johann J.; Spaltenstein, Andrew; Landavazo, Antonio; Chestnut, William; Aulabaugh, Ann; Taylor, Lester C. E.; Daniels, Alejandro J.
CORPORATE SOURCE: Wellcome Res. Labs., Research Triangle Park, NC, 27709, USA
SOURCE: International Journal of Peptide & Protein Research (1996), 47(3), 161-6
CODEN: IJPPC3; ISSN: 0367-8377
PUBLISHER: Munksgaard
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Oxidation of nonapeptide dithiol H-Ile-Cys-Pro-Cys-Tyr-Arg-Leu-Arg-Tyr-NH2 with K3Fe(CN)6 leads to either monomeric disulfide (4) or antiparallel and parallel dimeric disulfides (3a and 3b) depending upon reaction conditions. When exposed to small amts. of thiols or cyanide in aqueous solution, these three species interconvert to an equilibrium mixture of 2:1:8 (3a:3b:4).

IT **177582-22-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation, structure and stability of novel dimeric peptide disulfides)

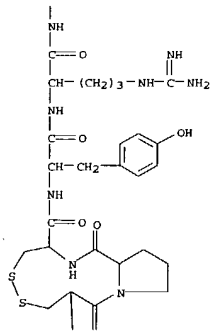
RN 177582-22-8 CAPLUS
CN L-Tyrosinamide, L-isoleucyl-L-cysteinyl-L-prolyl-L-cysteinyl-L-tyrosyl-L-arginyl-L-leucyl-L-arginyl-, cyclic (2→4)-disulfide (9CI) (CA INDEX NAME)

PAGE 1-A

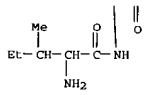


L4 ANSWER 250 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 2-A



PAGE 3-A



L4 ANSWER 251 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1996:177848 CAPLUS
DOCUMENT NUMBER: 124:232269
TITLE: Quinoline derivatives as tachykinin NK3 receptor antagonists
INVENTOR(S): Farina, Carlo; Giardina, Giuseppe Arnaldo Mari; Grugni, Mario; Raveglia, Luca Francesco
PATENT ASSIGNEE(S): Smithkline Beecham Farmaceutici S.P.A., Italy
SOURCE: PCT Int. Appl., 95 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9532948	A1	19951207	WO 1995-EP2000	19950523
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2191352	AA	19951207	CA 1995-2191352	19950523
CA 2191352	C	20010130		
CA 2257662	AA	19951207	CA 1995-2257662	19950523
AU 9526164	A1	19951221	AU 1995-26164	19950523
AU 699319	B2	19981203		
HU 76286	A2	19970728	HU 1996-3262	19950523
CN 1156451	A	19970806	CN 1995-194338	19950523
CN 1092642	B	20021016		
BR 9507788	A	19970923	BR 1995-7788	19950523
EP 804419	A1	19971105	EP 1995-920894	19950523
EP 804419	B1	20030806		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI				
JP 10500697	T2	19980120	JP 1996-500287	19950523
RO 114445	B3	19990430	RO 1996-2234	19950523
EP 940391	A2	19990908	EP 1998-204483	19950523
EP 940391	A3	19991110		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI				
JP 2000026314	A2	20000125	JP 1999-172597	19950523
NZ 329979	A	20000728	NZ 1995-329979	19950523
RU 2155754	C2	20000910	RU 1996-124804	19950523
JP 2002179594	A2	20020626	JP 2001-326622	19950523
SK 282721	B6	20021106	SK 1996-1514	19950523
SK 282722	B6	20021106	SK 1999-47	19950523
CZ 291476	B6	20030312	CZ 1996-3470	19950523
AT 246677	E	20030815	AT 1995-920894	19950523
PL 186075	B1	20031031	PL 1995-317381	19950523
PT 804419	T	20031231	PT 1995-920894	19950523
PL 186665	B1	20040227	PL 1995-341889	19950523
ZA 9504269	A	19960514	ZA 1995-4269	19950525
US 5811553	A	19980922	US 1995-450438	19950525

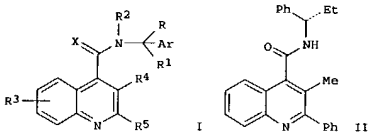
L4 ANSWER 251 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

US 6608083	B1	20030819	US 1995-450437	19950525
TW 427977	B	20010401	TW 1995-84105319	19950526
TW 533199	B	20030521	TW 1999-88121625	19950526
BG 64004	B1	20030930	BG 1996-101008	19961125
FI 9604712	A	19970123	FI 1996-4712	19961126
NO 9605036	A	19970124	NO 1996-5036	19961126
CN 1276211	A	20001213	CN 1999-100978	19990115
AU 9912162	A1	19990325	AU 1999-12162	19990119
FI 9900268	A	19990210	FI 1999-268	19990210
NO 9901813	A	19970124	NO 1999-1813	19990416
US 2003236281	A1	20031225	US 2001-867133	20010529
CN 1428145	A	20030709	CN 2002-107941	20020318

PRIORITY APPLN. INFO.:

IT 1994-MI1099	A	19940527
IT 1995-MI494	A	19950314
AU 1995-26164	A3	19950523
CA 1995-2191352	A	19950523
EP 1995-920894	A3	19950523
JP 1996-500287	A	19950523
NZ 1995-287442	A1	19950523
WO 1995-EP2000	W	19950523
US 1995-450437	A3	19950525

OTHER SOURCE(S): MARPAT 124:232269
GI

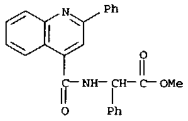


AB NK3 receptor antagonists I [Ar = (un)substituted Ph, naphthyl, cycloalkadienyl, heteroaryl; R = (un)substituted alkyl, cycloalkyl, (un)substituted Ph, phenylalkyl, or heteroaryl, CO2H and derivs., etc.; R1, R2 = H, alkyl; or R1R2 = (CH2)3-5; or RR1 = (CH2)2-5; R3, R4 = H, alkyl, alkenyl, aryl, alkoxy, OH, halo, NO2, amino, etc.; R5 = alkyl, cycloalkyl, (un)substituted (hetero)aryl; X = O, S, N(CN)] are useful in treating pulmonary, CNS, and neurodegenerative disorders, etc. Approx. 115 compds. were prepared For example, amidation of 3-methyl-2-phenylquinoline-4-carbonyl chloride with (R)-α-ethylbenzylamine gave title compound II in 58% yield. II had IC50 of 5.6 nM for displacement of [3H]-senktide from guinea-pig cortical NK3 receptors. Antagonist activity of I was shown by inhibition of senktide-induced contraction of guinea-pig ileum.

IT **174635-51-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of quinolinecarboxamide derivs. as tachykinin NK3 receptor antagonists)

RN 174635-51-9 CAPLUS
CN Benzeneacetic acid, α-[[(2-phenyl-4-quinolinyl)carbonyl]amino]-, methyl ester (9CI) (CA INDEX NAME)

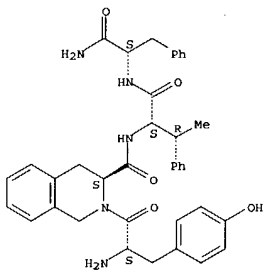
L4 ANSWER 251 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 252 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:12187 CAPLUS
DOCUMENT NUMBER: 124:202986
TITLE: Synthesis of the diastereomers of β-Me-Tyr and B-Me-Phe and their effect on the biological properties of the delta opioid receptor antagonist TIPP
AUTHOR(S): Mannekens, Els; Tourwe, Dirk; Vanderstichele, Sylvia; Nguyen Thi Diem, Trang; Toth, Geza; Peter, Antal; Chung, Nga N.; Schiller, Peter W.
CORPORATE SOURCE: Org. Chem., Free Univ., Brussels, B-1050, Belg.
SOURCE: Letters in Peptide Science (1995), 2(3/4), 190-2
CODEN: LPSCEM; ISSN: 0929-5666
PUBLISHER: ESCOM
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In order to influence side chain conformations and to increase the μ-agonist properties of the δ-selective opioid receptor δ-antagonist H-Tyr-Tic-Phe-Phe-NH2 (TIPP; Tic = 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid), residues Tyr1, Phe3 and Phe4 were replaced by their β-methyl-substituted stereoisomers. Synthesis of β-Me-Tyr was carried out in a stereoselective way. Incorporation of the modified amino acids was performed by solid-phase methods. Receptor binding data and GPI and MVD bioassays were obtained for all stereoisomers, in general showing equal or slightly increased potencies. In the [(R,S)β-Me-Phe3] analog, the introduction of the β-Me substituent restores signal transduction.
IT **174147-54-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of β-methyltyrosine and β-methylphenylalanine and their effect on the opioid antagonistic activity of TIPP)
RN 174147-54-7 CAPLUS
CN L-Phenylalaninamide, L-tyrosyl-(3S)-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-(βR)-β-methyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

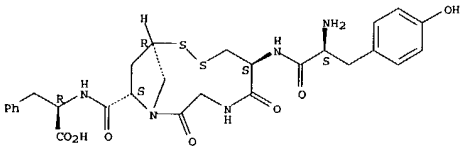
Absolute stereochemistry.

L4 ANSWER 252 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 253 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1996:12183 CAPLUS
DOCUMENT NUMBER: 124:135903
TITLE: Towards nonpeptide agonists: design of 'true' peptidomimetics
AUTHOR(S): Nikiforovich, Gregory V.
CORPORATE SOURCE: Cent. Mol. Design, Washington Univ., St. Louis, MO, 63130, USA
SOURCE: Letters in Peptide Science (1995), 2(3/4), 172-6
CODEN: LPSCEM; ISSN: 0929-5666
PUBLISHER: ESCOM
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This paper outlines the basic strategy to design 'true' peptidomimetics, i.e., nonpeptide compds. that bind to the same receptor site as the parent peptide. Design of highly selective and potent agonist analogs of δ-opioid peptides based on development of the 3D model for the δ-opioid pharmacophore is described. The design employed mol. modeling in combination with synthesis, biol. testing, NMR spectroscopy and x-ray studies. The designed compds. were able to bind the δ-opioid receptors with affinities and selectivities comparable to those for DPDPE, a well-known δ-selective agonist. They also showed moderate δ-agonistic activity.
IT **173555-72-1**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(design of δ-opioid agonists from peptidomimetics in relation to conformation)
RN 173555-72-1 CAPLUS
CN D-Phenylalanine, L-tyrosyl-D-cysteinylglycyl-trans-4-mercapto-L-prolyl-, cyclic (2→4)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 254 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:998406 CAPLUS
DOCUMENT NUMBER: 124:203098
TITLE: Preparation of peptide factor Xa inhibitors as antithrombotics.
INVENTOR(S): Al-Obeidi, Fahad; Lebl, Michal; Ostrem, James A.; Safar, Pavel; Stierandova, Alena; Strop, Peter; Walser, Armin
PATENT ASSIGNEE(S): Selectide Corp., USA
SOURCE: PCT Int. Appl., 107 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

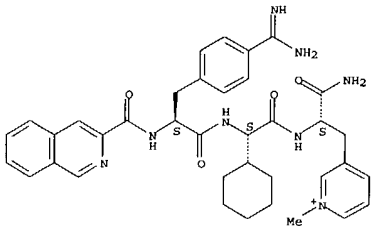
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9529189	A1	19951102	WO 1995-US5268	19950425
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2186497	AA	19951102	CA 1995-2186497	19950425
AU 9523683	A1	19951116	AU 1995-23683	19950425
AU 707653	B2	19990715		
ZA 9503361	A	19960112	ZA 1995-3361	19950425
EP 758341	A1	19970219	EP 1995-917736	19950425
EP 758341	B1	20040324		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1147261	A	19970409	CN 1995-192811	19950425
HU 76346	A2	19970828	HU 1996-2954	19950425
JP 10503477	T2	19980331	JP 1995-527853	19950425
RU 2152954	C1	20000720	RU 1996-122647	19950425
EE 3973	B1	20030217	EE 1996-146	19950425
EP 1384725	A2	20040128	EP 2003-21617	19950425
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
IL 113505	A1	19991231	IL 1995-113505	19950426
TW 409129	B	20001021	TW 1995-84104681	19950511
FI 9604317	A	19961025	FI 1996-4317	19961025
NO 9604553	A	19961227	NO 1996-4553	19961025
LT 4218	B	19970925	LT 1996-151	19961025
LV 11740	B	19971220	LV 1996-410	19961115
US 5849510	A	19981215	US 1997-947794	19971008

PRIORITY APPLN. INFO.: US 1994-233054 A 19940426
EP 1995-917736 A3 19950425
US 1995-428404 B1 19950425
WO 1995-US5268 W 19950425

OTHER SOURCE(S): MARPAT 124:203098
AB A1-A2-(A3)m-B [m = 0, 1; A1 = R1-R2-R3; A2 = R4-R5-R6; A3 = R7-R8-R9; R1 = (substituted) 1-20 amino acid residues, R11CO, R11R12X; X = N, CH, NCO; R11, R12 = H, alkyl, acyl, aryl, aralkyl, protecting group; R2 = CR99R100; R99, R100 = H, (substituted) alkyl, aralkyl, heteroaralkyl, heteroaryl; R3 = CO, CH2, CHR99CO, etc.; R4 = CH2, imino; R5 = CR201R202; R201, R202 = H, (substituted) alkyl, aryl, aralkyl; R6 = CO, CH2, CHR99CO; R7 = (substituted) R4; R8 = CR210R211; R210, R211 = H, (substituted) alkyl, alkylaryl, heterocyclyl; R9 = CO, CH2, CHR99CO; B = (substituted) 1-20 amino acid residues, amino, OH, alkoxy, acyloxy, etc.; with provisos], were prepared Thus, Ac-Tyr-Chg-Arg-NH2 (Chg = cyclohexylglycyl) inhibited

L4 ANSWER 254 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
coagulation in human plasma with EC50 = 2.5 μM.
IT **174132-79-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptide factor Xa inhibitors as antithrombotics)
RN 174132-79-7 CAPLUS
CN L-Alaninamide, 4-(aminoiminomethyl)-N-(3-isoquinolinylcarbonyl)-L-phenylalanyl-L-2-cyclohexylglycyl-3-(1-methylpyridinium-3-yl)- (9CI) (CA INDEX NAME)

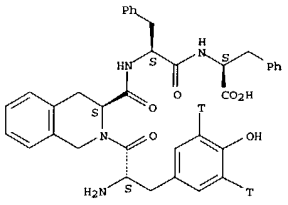
Absolute stereochemistry.



L4 ANSWER 255 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:911314 CAPLUS
DOCUMENT NUMBER: 124:87771
TITLE: Synthesis, tritium labeling and binding characterization of new delta opioid receptor selective antagonists, TIPP and TIPP[ψ]
AUTHOR(S): Toth, G.; Nevin, S.; Borsodi, A.; Nguyen, T. M. -D.; Schiller, P.
CORPORATE SOURCE: Biological Research Center, Hungarian Academy Sciences, Szeged, H-6701, Hung.
SOURCE: Synthesis and Applications of Isotopically Labelled Compounds 1994, Proceedings of the International Symposium, 5th, Strasbourg, June 20-24, 1994 (1995), Meeting Date 1994, 141-4. Editor(s): Allen, John; Voges, Rolf. Wiley: Chichester, UK.
CODEN: 61UMAF
DOCUMENT TYPE: Conference
LANGUAGE: English
AB A symposium report on the preparation and δ opioid receptor binding affinities of the title tritiated peptide antagonists H-Tyr-Tic-Phe-Phe-OH (TIPP; Tic = 1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid) and its analog TIPP[ψ] with a pseudopeptide bond between Tic and Phe (H-Tyr-Tic[CH2NH]Phe-Phe-OH), prepared to obtain a more stable ligand under radioreceptor assay conditions. The two peptides were labeled by tritium using precursors containing 3,5-diiodotyrosine. After catalytic dehalogenation with tritium gas, the crude labeled peptides were purified by HPLC. Specific radioactivity was 1.87 TBq/mmol for TIPP and 1.76 TBq/mmol for TIPP[ψ]. The tritiated ligands labeled rat brain membrane binding sites with Kd values under the nanomolar range and Bmax values were found to be 82 and 105 fmol/mg protein for TIPP and TIPP[ψ], resp. Both tritiated ligands proved to be highly selective for δ opioid receptors in binding competition expts.
IT **172490-62-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation, tritium labeling and binding characterization of new δ opioid receptor selective antagonist peptides)
RN 172490-62-9 CAPLUS
CN L-Phenylalanine, L-tyrosyl-3,5-t2-L-1,2,3,4-tetrahydro-3-isoquinolinecarbonyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

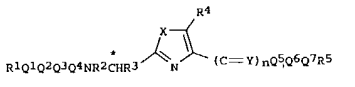
L4 ANSWER 255 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 256 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:804314 CAPLUS
DOCUMENT NUMBER: 123:228900
TITLE: Preparation of azole-fused peptides as substance P antagonists and analgesics.
INVENTOR(S): Morgan, Barry A.; Gordon, Thomas D.; Hansen, Philip E.; Singh, Jasbir
PATENT ASSIGNEE(S): Sterling Winthrop Inc., USA
SOURCE: U.S., 34 pp. Cont. of U.S. Ser. No. 131,706, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5378803	A	19950103	US 1992-912949	19920710
PRIORITY APPLN. INFO.:			US 1987-131706	19871211

OTHER SOURCE(S): MARPAT 123:228900
GI



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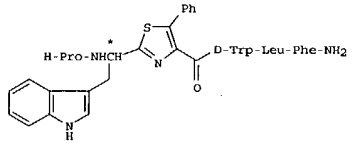


II

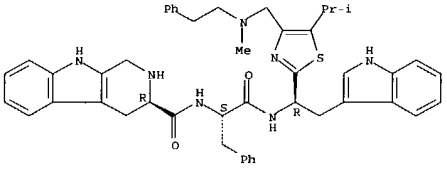
AB Title compds. [I; Q1 = Pro, bond; Q2 = Pro, D-Trp, bond; Q3 = Pro, D-Trp, Phe, (R)-(2,3,4,9-tetrahydro)-1H-pyrido[3,4-b]indol-2-yl-3-carbonyl, bond; Q4 = Pro, D-Trp, Phe, bond; Q5 = D-Trp, Phe, bond; Q6 = Leu, Met, bond; Q7 = Phe, N-MePhe, Met, bond; R1 = H, Z, BOC; R2 = H; R3 = Me2CH, Me2CHCH2, H2N(CH2)4, PhCH2, 4-HOC6H4CH2, pyridylmethyl, (1H-indol-3-yl)methyl; R2R3 = atoms to form 2,3,4,9-tetrahydro-1H-pyrido[3,4-b]indol-2,3-diyl; R5 = H, OH or alkali metal salt thereof, MeO, EtO, amino, etc.; X = oxa thia, imido; Y = oxo, H2; n = 0,1; starred center is L or D; with a proviso], were prepared Thus, title compound (II; starred center has D-configuration), prepared via thionation of Z-D-Trp-NH2 with P2S5 and cyclocondensation of the product with Et 3-chloro-2-oxo-3-phenylpropionate, antagonized substance P in the guinea pig ileum test with pA2 = 7.3, and in the mouse acetylcholine-induced writhing test showed intrathecal ED50 = 0.78 μg/mouse.
IT **167982-54-9P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

L4 ANSWER 256 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
(prepn. of azole-fused peptides as substance P antagonists and analgesics)
RN 167982-54-9 CAPLUS
CN 1H-Pyrido[3,4-b]indole-3-carboxamide, 2,3,4,9-tetrahydro-N-[2-[[2-(1H-indol-3-yl)-1-[5-(1-methylethyl)-4-[[methyl(2-phenylethyl)amino]methyl]-2-thiazolyl]ethyl]amino]-2-oxo-1-(phenylmethyl)ethyl]-, [3R-[3R*[S*(R*)]]]-, phosphate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 167982-53-8
CMF C47 H51 N7 O2 S

Absolute stereochemistry.



CM 2

CRN 7664-38-2
CMF H3 O4 P

L4 ANSWER 257 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:801429 CAPLUS
DOCUMENT NUMBER: 123:256711
TITLE: Preparation of gastrin and CCK receptor ligands
INVENTOR(S): Kalindjian, Sarkis Barret; Steel, Katherine Isobel Mary; Pether, Michael John; Davies, Jonathan Michael Richard; Low, Caroline Minli Rachel; Hudson, Martin Lyn; Buck, Ildiko Maria; McDonald, Iain Mair; Dunstone, David John; Tozer, Matthew John
PATENT ASSIGNEE(S): James Black Foundation Ltd., UK
SOURCE: PCT Int. Appl., 124 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9504720	A2	19950216	WO 1994-GB1741	19940809
WO 9504720	A3	19950803		
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN				
RW: KE, MW, SD, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9473478	A1	19950228	AU 1994-73478	19940809
AU 682051	B2	19970918		
EP 720601	A1	19960710	EP 1994-922318	19940809
EP 720601	B1	20001025		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 09502430	T2	19970311	JP 1994-506306	19940809
HU 75301	A2	19970528	HU 1996-70	19940809
AT 197146	E	20001115	AT 1994-922318	19940809
ES 2152989	T3	20010216	ES 1994-922318	19940809
PT 720601	T	20010228	PT 1994-94922318	19940809
PL 181782	B1	20010928	PL 1994-312960	19940809
ZA 9405998	A	19960212	ZA 1994-5998	19940810
GB 2290539	A1	19960103	GB 1995-2503	19950209
WO 9532949	A1	19951207	WO 1995-GB1194	19950525
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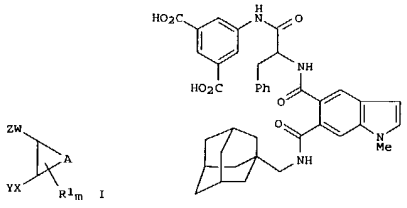
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9525342	A1	19951221	AU 1995-25342	19950525
EP 763026	A1	19970319	EP 1995-919561	19950525
EP 763026	B1	20030326		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10504525	T2	19980506	JP 1995-500483	19950525
AT 235470	E	20030415	AT 1995-919561	19950525
ZA 9504315	A	19961126	ZA 1995-4315	19950526
NO 9600488	A	19960315	NO 1996-488	19960206
FI 9600572	A	19960207	FI 1996-572	19960207
US 5795907	A	19980818	US 1996-583008	19960318

L4 ANSWER 257 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

US 5912260	A	19990615	US 1996-737725	19961219
US 5919829	A	19990706	US 1998-64849	19980423
GR 3035100	T3	20010330	GR 2000-402788	20001218

PRIORITY APPLN. INFO.:
GB 1993-16608 A 19930810
GB 1994-10688 A 19940527
WO 1994-GB1741 W 19940809
GB 1995-2503 A 19950209
WO 1995-GB1194 W 19950525

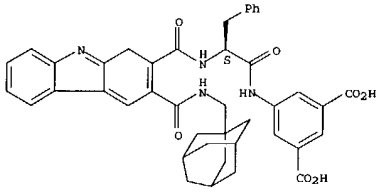
OTHER SOURCE(S): MARPAT 123:256711
GI



AB Title compds. [e.g. I; A = atoms to complete a bicyclic ring system; R1 = halo, NH2, cyano, OH, alkyl, CO2H, etc.; 1 of X, W = CO and the other = CO, SO, SO2; Y = NR3R4, hydrocarbyloxy, etc.; R3 = H, hydrocarbyl, etc.; R4 = H, alkyl, (un) esterified CH2CO2H; Z = OH, alkoxy, OPh, (un)substituted NH2, NHZ1R, etc.; R = H, cyano, alkyl, CH2OH, CO2H, etc.; Z1 = alkylene; m = 0-6] were prepared Thus, 4-methylphthalic anhydride was converted in 6 steps to indole-5,6-dicarboxylic anhydride which was amidated by adamantane-1-methylamine and the product amidated by (S)-3,5-(PhH2CO2C)2C6H3NHCOCH(NH2)CH2Ph (preparation given) to give, in 2 addnl. steps, title compound (S)-II the di-N-methyl-D-glucamine salt of which had pKi of 9.4 for binding at mouse cortex CCKB receptors in vitro.
IT **167991-35-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of gastrin and CCK receptor ligands)
RN 167991-35-7 CAPLUS
CN 1,3-Benzenedicarboxylic acid, 5-[[1-oxo-3-phenyl-2-[[[3-[[(tricyclo[3.3.1.13,7]dec-1-ylmethyl)amino]carbonyl]-1H-carbazol-2-yl]carbonyl]amino]propyl]amino]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

L4 ANSWER 257 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)



L4 ANSWER 258 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:789155 CAPLUS
DOCUMENT NUMBER: 123:199414
TITLE: Preparation of peptidyllactol derivatives as inhibitors of cathepsin L.
INVENTOR(S): Sohda, Takashi; Fujisawa, Yukio; Oi, Satoru; Mizoguchi, Junji
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: Eur. Pat. Appl., 54 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 641800	A1	19950308	EP 1994-113669	19940901
EP 641800	B1	20020116		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
NO 9403210	A	19950306	NO 1994-3210	19940830
JP 08104685	A2	19960423	JP 1994-208981	19940901
AT 212036	E	20020215	AT 1994-113669	19940901
CA 2131397	AA	19950304	CA 1994-2131397	19940902
FI 9404040	A	19950304	FI 1994-4040	19940902
AU 9471682	A1	19950316	AU 1994-71682	19940902
AU 678493	B2	19970529		
HU 68717	A2	19950728	HU 1994-2536	19940902
CN 1106001	A	19950802	CN 1994-115669	19940902
US 5496834	A	19960305	US 1994-300738	19940902

PRIORITY APPLN. INFO.: JP 1993-219655 A 19930903
JP 1994-168501 A 19940720
JP 1994-190385 A 19940812

OTHER SOURCE(S): MARPAT 123:199414
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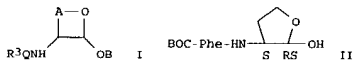
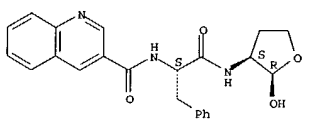


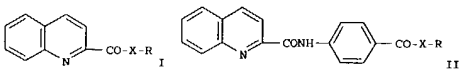
AB Title compds. [I; Q = 1-2 (substituted) amino acid residues; R3 = (esterified) carboxyl, acyl; A = alkylene; B = H, (substituted) alkyl, acyl], were prepared Thus, N-benzyloxycarbonylhomoserine, 1-hydroxybenzotriazole, and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide were stirred 14 h in DMF at ice temp-room temperature to give 84.3% (S)-3-(N-benzyloxycarbonylamino)tetrahydrofuran-2-one. This was hydrogenolyzed in EtOH over Pd/C and the product was stirred with BOC-Phe-OH, 1-hydroxybenzotriazole, and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide in DMF to give 78.3% (S)-3-(N-tert-butoxycarbonylphenylalanylamino)tetrahydrofuran-2-one. The latter in THF was treated with DIBAL in PhMe at -72° to give 37.5% title compound (II). I inhibited cathepsin L with IC50 = 6.9 + 10-7-8.0 + 10-9 M, and at 10-30 μM gave 26-82% inhibition of bone resorption in

L4 ANSWER 258 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)
rat fetuses according to the method of Raisz.
IT **167766-31-6P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of peptidyllactol derivs. as inhibitors of cathepsin L)
RN 167766-31-6 CAPLUS
CN 3-Quinolinecarboxamide, N-[2-oxo-1-(phenylmethyl)-2-[(tetrahydro-2-hydroxy-3-furanyl)amino]ethyl]-, [2R-[2α,3α(S*)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

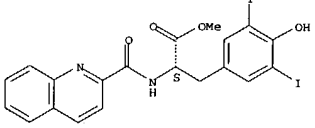


L4 ANSWER 259 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:723478 CAPLUS
DOCUMENT NUMBER: 123:340785
TITLE: Synthesis of new quinolin-2-carbonyl-N-amino acid derivatives with evaluation of their antimicrobial activity
AUTHOR(S): Shalaby, A.M.; Kassem, E.M.M.; Farrag, H.A.
CORPORATE SOURCE: National Research Centre, Cairo, Egypt
SOURCE: Proceedings of the Pakistan Academy of Sciences (1994), 31(3), 163-73
CODEN: PKSPAW; ISSN: 0377-2969
PUBLISHER: Pakistan Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB 2-Quinolinecarbonyl chloride and 4-(2-quinolinecarbonylamino)benzoyl chloride (I and II; X = bond, R = Cl) reacted with amino acid esters H-X-OMe (X = Gly, L-Val, DL-Met, L-3,5-diiodotyrosine) in THF to give the corresponding amides II (R = OMe), which on hydrolysis gave the free acids II (R = OH). Condensation of II (R = OMe) with N2H4 gave the corresponding hydrazides II (R = NHNH2), which in turn were condensed with aromatic aldehydes R1CHO [R1 = 4-pyridyl, (MeO)3C6H2] to give the Schiff bases II (R = NHN:CHR1). The antimicrobial activity of the prepared compds. was also studied.
IT **170488-13-8P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(preparation and antimicrobial activity of new (quinolinecarbonyl)amino acid derivs.)
RN 170488-13-8 CAPLUS
CN L-Tyrosine, 3,5-diiodo-N-(2-quinolinylcarbonyl)-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

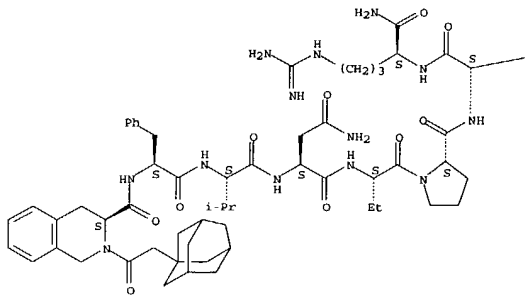


L4 ANSWER 260 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 1995:657214 CAPLUS
DOCUMENT NUMBER: 123:314483
TITLE: Synthesis and some pharmacological properties of seven new analogs of Aaa-D-Tyr(Et)-Phe-Val-Asn-Abu-Pro-Arg-Arg-NH2, a potent linear antagonist of V2 receptors
AUTHOR(S): Czaja, M.; Konieczna, E.; Wierzba, T.; Juzwa, W.; Lammek, B.
CORPORATE SOURCE: Dep. Chem., Univ. Gdansk, Gdansk, 80-952, Pol.
SOURCE: Polish Journal of Chemistry (1995), 69(4), 552-8
CODEN: PJCHDQ; ISSN: 0137-5083
PUBLISHER: Polish Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Seven new analogs of potent V2/V1 antagonist adamantaneacetyl-D-Tyr(Et)-Phe-Val-Asn-Abu-Pro-Arg-Arg-NH2 (I) were synthesized. Four of them were designed by substitution of positions 2 or 3 with L- or D-1,2,3,4-tetrahydroisoquinolinecarboxylic acid. One peptide was designed by replacement of Phe3 residue by L-β-thienylalanine. Two compds. have a disulfide bridge on the C-terminal end of model peptide I. The anti-antidiuretic activity of the analogs was evaluated by their ability to inhibit the antidiuretic effect of endogenous arginine-vasopressin (AVP). The antipressor potency of the peptides was assayed by their ability to inhibit the pressor response to exogenous AVP. The modifications proposed are incompatible with biol. potency, particularly anti-V2 activity. Nevertheless, two of the new analogs are potent vasopressor antagonists.
IT **169824-40-2P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(synthesis and anti-antidiuretic and antipressor activities of analogs of potent linear antagonist of V2 receptors)
RN 169824-40-2 CAPLUS
CN L-Argininamide, N-[[1,2,3,4-tetrahydro-2-(tricyclo[3.3.1.13,7]dec-1-ylacetyl)-3-isoquinolinyl]carbonyl]-L-phenylalanyl-L-valyl-L-asparaginyl-L-2-aminobutanoyl-L-prolyl-L-arginyl-, (S)- (9CI) (CA INDEX NAME)

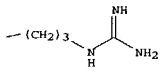
Absolute stereochemistry.

L4 ANSWER 260 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN (Continued)

PAGE 1-A



PAGE 1-B



L4 ANSWER 261 OF 261 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 1995:633575 CAPLUS
DOCUMENT NUMBER: 123:314476
TITLE: Acid catalysis in the formation of dioxopiperazines from peptides containing tetrahydroisoquinoline-3-carboxylic acid at position 2
AUTHOR(S): Capasso, Sante; Sica, Filomena; Mazzarella, Lelio; Balboni, Gianfranco; Guerrini, Remo; Salvadori, Severo
CORPORATE SOURCE: Dep. Chem., Univ. Naples "Federico II, Naples, Italy
SOURCE: International Journal of Peptide & Protein Research (1995), 45(6), 567-73
CODEN: IJPPC3; ISSN: 0367-8377
PUBLISHER: Munksgaard
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The kinetics of the spontaneous formation of 2,5-dioxopiperazines from peptides containing the Tic (1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid) residue in the 2-position of the sequence has been studied in DMSO and water solution The reaction is first order in Tic-peptide and subject to general-acid catalysis. Moreover, only the fraction of peptide having the amino terminal group in the deprotonated state reacts with appreciable rate. In pure organic solvent, and in aqueous solution with low buffer concentration, the degradation reaction of Tic-peptides is very low; at 20° for the peptide H-Tyr-Tic-Phe-Phe-NH2, in DMSO and in neutral water in the absence of buffer, the half-lives (t1/2) are 3 + 104 and 1.2 + 104 h, resp. The addition of carboxylic acids or buffers to the reaction solns. markedly increases the reaction rate; in 0.01 M HAc in DMSO and in 0.1 M phosphate buffer in water, pH 7.1, t1/2 values for the tetrapeptide are 61 and 121 h, resp.

IT **169611-83-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(acid catalysis in formation of dioxopiperazines from peptides containing tetrahydroisoquinolinecarboxylic acid)

RN 169611-83-0 CAPLUS
CN L-Phenylalaninamide, N-[[2-[(1,1-dimethylethoxy)carbonyl]-1,2,3,4-tetrahydro-3-isoquinolinyl]carbonyl]-L-phenylalanyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.